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Prevalence of Frailty and Pre-Frailty among Community Dwelling Older Adults in Low and Middle Income Countries: A Systematic Review and Meta-Analysis

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Abstract

Objective: To systematically review the research conducted on prevalence of frailty and pre-frailty among community dwelling older adults in low and middle income countries (LMICs) and to estimate the pooled prevalence of frailty and pre-frailty in community dwelling older adults in LMICs.

Design: Systematic review and meta-analysis. PROSPERO registration number is CRD42016036083.

Data sources: Searches of MEDLINE, EMBASE, AMED, Web of Science, CINAHL and LILACS databases from their inception to June, 23 2016.

Setting: Low and middle income countries.

Participants: Community dwelling older adults aged 60 years and above.

Results: We screened 5218 citations and 44 studies were included. Thirty six and 32 studies were included in the frailty and pre-frailty meta-analysis respectively. The majority of studies were from upper middle income countries. No studies were available from low income countries. The prevalence of frailty varied from 5.2% (China) to 51.4% (Cuba) and prevalence of pre-frailty ranged from 20.4% (Brazil) to 71.3% (Colombia) for the studies with populations aged 60, 65 or 70 and over. The pooled prevalence of frailty was 18.0% (95% CI=15.0-22.0%, I^2 =99.2) and pre-frailty was 48.0% (95% CI= 45.0-51.0%, I^2 =96.5). The wide variation in prevalence rates across studies was largely explained by differences in frailty assessment method and the geographic region.

Conclusion: The prevalence of frailty and pre-frailty appears higher in community dwelling older adults in upper middle income countries compared to high income countries, which has important implications for healthcare planning.

Key words: Ageing, Epidemiology, Systematic review

Strengths and limitations of this study

- This is the first systematic review and meta-analysis of the prevalence of frailty and pre-frailty among community dwelling older adults in low and middle income countries.
- We conducted a comprehensive literature search in six electronic databases with a comprehensive search strategy, including a regional database (LILACS) to capture studies published regionally.
- No language restriction was imposed.
- Sub group analysis of prevalence of frailty and pre-frailty was performed with substantial number of studies, and meta-regression technique was used to identify the sources of heterogeneity between the studies.
- We did not include the grey literature in this review.

INTRODUCTION

Population ageing is not confined to High Income Countries (HICs). People in Low and Middle Income Countries (LMICs) have increasing life expectancy with the advancement of health care services.[1] The pace of population ageing is faster in LMICs compared to HICs.[2] This creates an additional burden for these countries with growing economies as they have to tackle health, social and welfare issues associated with ageing populations.

Frailty is a health problem of older age with no universally agreed conceptual or operational definition. However, there is a common agreement that frailty is an important clinically identifiable state that increases the vulnerability to adverse outcomes due to the decline in reserve and functions in multiple physiological systems.[3] The Fried phenotype of frailty, comprised of five phenotypic criteria (unintentional weight loss, self-reported exhaustion, weakness, slowness and low physical activity)[4] and the frailty index, (comprised of a list of deficits),[5] are the most frequently used frailty assessment methods in the literature.[6]

Longitudinal studies have identified several negative outcomes associated with frailty which can have a huge impact on individual lives and society as a whole. These include falls, worsening mobility, disability, hospitalization and increased risk of mortality.[4 5 7 8] Evidence is emerging that frailty as a dynamic state with transitions between frailty statuses; frailty, pre-frailty (intermediate state between frailty and non-frailty) and non- frailty,[9-11] and there is potential for interventions to improve the health of frail older adults.

A substantial amount of research on frailty has been conducted in HICs. According to a systematic review conducted in 2012, the weighted prevalence of frailty in HICs is 10.7% and pre-frailty is 41.6%.[12] There is some suggestion of a socio-economic gradient in frailty between HICs; one study from 15 European countries reported a lower mean frailty index in North and Western Europe compared to lower income countries in South and Eastern

Europe.[13] In addition, the survival of frail older people was higher in countries with a higher relative income within Europe.[13]

It is possible that the prevalence of frailty in LMICs is higher than HICs, given a steeper gradient in income. Alternatively the prevalence may be lower with a reduced life expectancy of older people in LMICs. There are no studies collating all the epidemiological findings available from LMICs to examine the burden of frailty in these countries. This is important to inform health care planning in these countries in the context of world-wide population ageing. The aim of this study was to conduct a systematic review and meta-analysis on prevalence of frailty and pre-frailty among community dwelling older adults in Low and Middle Income Countries.

METHODS

Search Strategy and selection criteria

We performed a comprehensive structured search in six electronic bibliographic databases. MEDLINE, EMBASE and AMED databases using OvidSP interface, Web of Science Core Collection, CINAHL Plus and LILACS databases were searched from their inception to 23, June 2016. Two concepts; "frailty" and "low and middle income countries" were used to develop the electronic search strategy. The example Low and Middle Income Country filters developed by Cochrane organization in 2012 was used with slight modifications.[14] The World Bank country classification of 2016[15] which is based on 2014 economic data was used to identify the countries that switched from low and middle income to high income countries in 2016. Studies in these countries were included only if the time period for data collection was before the transition to high income status. The electronic search strategy was first developed for MEDLINE (appendix A, supplementary file) and then adapted accordingly to other databases. The electronic search strategy was developed with the support of specialist

librarian (SP). Additionally reference lists of the selected articles were scanned and citation searches were performed in the Web of Science. The search was limited to full text articles as study quality assessment requires a detailed description on the methodology. No language restriction was imposed on the search.

The condition studied was frailty measured by any assessment method. The review was restricted to studies with community dwelling older adults aged 60 and above living in the LMICs. Studies with institutionalized or hospitalized adults, nursing home residents, outpatients of primary or secondary care clinics, or older adults belonging to specific disease groups were excluded. Cross sectional studies conducted to assess the prevalence and associated factors of frailty, prospective follow-up studies that have baseline prevalence of frailty, cross sectional studies conducted to explore the association of frailty with some other health variable or disease (e.g. haemoglobin level, cardio vascular risk factors) were included in this review.

Identified citations were exported into EndNote X7 and duplicates were removed. In the first stage, the title and abstracts of the citations were screened against inclusion and exclusion criteria to identify potentially eligible citations. In the second stage, full-texts of potentially eligible articles were retrieved. Two reviewers (DS and SH) independently reviewed the full-text articles to identify the articles meeting eligibility criteria. If multiple studies were available from the same cohort, the study with a large sample and more information was included in the review. Disagreement between the reviewers was resolved through discussions and consulting senior researchers in the research team (KW, GR, and MW).

Study quality assessment and data extraction

Selected articles were subjected to a quality assessment. Methodological rigor of the articles was assessed using eight criteria proposed by Loney et al[16] for the critical appraisal of

prevalence literature. If a study achieved 3 criteria or less, it was excluded from the review. Study quality of all selected articles (47) was assessed by the first reviewer (DS). The second reviewer (SH) assessed the study quality of a random 10 percent of articles to check for discrepancies.

Data extraction included information on study background (authors and year of publication, data source, study setting, study period), characteristics of the population (percentage of females in the study population, mean age, age range, number of frail and pre-frail participants in the total sample, and by sex and age), study methodology (study design, effective sample, sampling technique, frailty assessment method) and study strengths and limitations. Authors were contacted requesting additional data required for sub group analysis.

Data analysis

The results of the systematic review are presented in tabular format and narratively synthesized. A random effects meta-analysis with 95% confidence intervals was performed to calculate the pooled prevalence of frailty and pre-frailty. A random effects model was chosen as there was considerable heterogeneity of the study characteristics including geography, frailty assessment method, and recruitment age. When a study has used multiple assessment methods of frailty, the prevalence presented using Fried phenotype was used for the meta-analysis as it was the most commonly used assessment method in the literature[17]. The analysis was performed on double arcsine transformed prevalence proportions to stabilize the variance[18]. Results were presented using forest plots. The Main meta-analysis and sub group analysis excluded two studies, one with recruitment age of 80+ as the study has not been given frailty prevalence cut-off and another study with recruitment age of 90+ years as it is a very old sample.

Cochran's Q statistic was used to assess heterogeneity between the studies. P<0.05 was considered as evidence of heterogeneity. The I^2 statistic was further used to quantify the magnitude of the heterogeneity. I^2 values of 25%, 50% and 75% were considered as low, moderate and high heterogeneity respectively[18]. Publication bias was assessed using funnel plots and Egger's test[19-21].

Sub group analysis of frailty and pre-frailty prevalence was performed according to the frailty assessment method (Fried phenotype with 5 criteria where weakness and slowness assessed objectively using grip strength and gait speed, Fried phenotype with 5 criteria where weakness and slowness assessed using self-reported questions (subjective), Fried phenotype with 4 criteria, Edmonton Frail Scale (EFS) and, frailty index). Two studies were excluded from the frailty and pre-frailty sub group analysis as those studies have used very different frailty assessment methods to that mentioned above (Study of Osteoporotic Fractures index (SOF) and Cuban frailty criteria). Further sub group analyses by sex, age group (60-64, 65-69, 70-74, 75-79, 80-84, 85+), age and sex were performed with studies which had employed the Fried phenotype with 5 criteria where weakness and slowness assessed using objective tests. Q test for heterogeneity was used to assess the difference of prevalence of frailty and pre-frailty across sub groups.

Random effects univariable and multivariable meta-regression were performed to identify the potential sources of heterogeneity (demographic, geographical and methodological) with all the studies included in the frailty meta-analysis that have data for all explanatory variables except two studies which used Study of Osteoporotic Fractures index (SOF) and Cuban frailty criteria. The following explanatory variables were included in the models; mean age, percentage of females in the study sample, geographic region (Asia, Europe and South America), study quality assessment score and frailty assessment method. All the variables

were included in the multivariable model irrespective of their significance (p value) in univariable analysis. Variables with P≤ 0.05 were considered as significant. All statistical analyses were performed in Stata version 12 (StataCorp LP, College Station, Texas, USA).

The systematic review protocol of this study registered in PROSPERO and number is (CRD42016036083). This systematic review and meta-analysis have been reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [22].

RESULTS

Study characteristics

The search yielded 7957 records, with 5218 records left after removing duplicates. Forty four studies meeting all eligibility criteria were included in the systematic review (figure 1). Thirty six and 32 studies were included in the meta-analysis of frailty and pre-frailty respectively.

Figure 1: Study selection

The study quality assessment score of the studies included ranged from 3.5 to 7.5, with a mean score of (standard deviation) 5.8 (1.15). Quality assessment results of the studies are presented in appendix B (supplementary file). The characteristics of the studies are described in appendix C (supplementary file). Thirty nine studies have been published between 2012 and 2016. The majority of the studies were from the South American region, predominantly from Brazil (n=18). Most of the studies had utilized data from large population based cross sectional or longitudinal studies on ageing.

The sample size of the studies varied (range 54 to 12373) and the minimum age of the study participants varied from 60 to 90 years. The minimum age at recruitment of the study participants was 60 years in 24 studies, 65 years in 15 studies, 70 years in 3 studies, 80 years in one study and 90 years in another. The percentage of females in the study samples varied

from 47.5% to 100.0%, with more than half of participants female in all except two studies. Thirty two studies reported the mean age (32/44) of the participants, which ranged from 68.7 to 76.6 years (after excluding a study with minimum recruitment age 90 years and above).

Studies used various frailty assessment methods. The Fried phenotype was the most extensively used method. Researchers had operationalized the Fried phenotype differently. We identified three broad categories based on the number of phenotypic criteria used and measures used to operationalize those criteria. Those are Fried phenotype with 5 criteria- weakness and slowness assessed using objective tests, Fried phenotype with 5 criteria- weakness and slowness assessed using self-reported questions (subjective) and Fried phenotype with only 4 criteria.

Prevalence of frailty and pre-frailty

Irrespective of the frailty assessment method, the prevalence of frailty varied from 5.2% in China (frailty index) to 51.4% in Cuba (Geriatric functional assessment scale) and prevalence of pre-frailty ranged from 20.4% in Brazil (EFS) to 71.3% in Colombia (Fried Phenotype with 5 criteria- weakness and slowness measured objectively) for the studies with minimum recruitment age 60 years, 65 years or 70 years and over. There was a one study in those aged 90 years+, reporting 61.8% participants as frail. When restricting to the studies that used Fried phenotype with five criteria and assessed the weakness and slowness objectively, the prevalence of frailty varied from 8.0% to 23.8% in Brazil. The prevalence of pre-frailty varied from 40.7% in Brazil to 71.3% in Colombia.

Pooled prevalence of frailty and pre-frailty

Fifty six prevalence estimates (36 studies), corresponding to a total of 62,566 community dwelling older adults, were included in the frailty meta-analysis. The random-effects pooled prevalence of frailty in community dwelling older adults was 18.0% (95% CI=15.0-22.0%, I^2

=99.2, p<0.01) (figure 2). Egger's test indicated the existence of potential publication bias (p<0.01). Forty two prevalence estimates (32 studies) corresponding to 35,246 participants were included in the pre-frailty meta-analysis. The random-effects pooled prevalence of pre-frailty in community dwelling older adults was 48.0% (95% CI= 45.0-51.0%, I^2 =96.5, p<0.01) (figure 3). Egger's test indicated no publication bias (p=0.6).

Figure 2: Random effects pooled prevalence of frailty among community dwelling older adults in middle income countries

Figure 3: Random effects pooled prevalence of pre-frailty among community dwelling older adults in middle income countries

Subgroup analyses

The pooled prevalence varied by the assessment method and the highest prevalence of frailty was reported for the EFS, 34.0% (95% CI= 30.0-39.0%, I^2 =40.2, p=0.15) and Fried phenotype with 5 criteria without objective assessment of weakness and slowness, 34.0% (95% CI= 28.0-40.0%, I^2 =98.3, p<0.01). The lowest prevalence of frailty was reported for Frailty phenotype with 5 criteria weakness and slowness assessed objectively, 12.0% (95% CI= 11.0-14.0%, I^2 =87.3, p<0.01) (appendix D, supplementary file). Forest plot for pooled prevalence of pre-frailty stratified by frailty assessment method is presented in appendix E (supplementary file).

Seventeen prevalence estimates were available from 17 studies using the same assessment method (Fried Phenotype with objective tests) for sex stratified analysis of prevalence of frailty and pre-frailty. In total there were 5,048 and 8,285 male and female participants respectively. The pooled prevalence of frailty in males was 11.0% (95% CI= 9.0-13.0%, I^2 =82.5, p<0.01) compared to 15.0% (95% CI= 12.0-17.0%, I^2 =86.6, p<0.01) in females. Frailty prevalence is significantly higher in females compared to males (Q=4.85, df=1,

p<0.001). The pooled prevalence of pre-frailty in males was 53.0% (95% CI=50.0-56.0%, I^2 =76.5, p<0.01) and females is 55.0% (95% CI= 53.0-58.0%, I^2 =80.6, p<0.01). Unlike in frailty, there is no statistically significant sex difference in pre-frailty (Q=1.55, df=1, p=0.2).

The prevalence of frailty increased gradually with advancing age (appendix F, supplementary file). The prevalence considerably increased after age 75 years. The prevalence of pre-frailty was around 55% in all age groups. An age related incremental rise in frailty was evident even after stratification by sex (appendix G, supplementary file). Prevalence of frailty was higher in females in all five year age bands. There was no age related trend for pre-frailty after stratification by sex (appendix H, supplementary file).

Meta-regression

After adjusting for all the other study characteristics in a multivariable meta-regression model, there remained statistically significant differences in frailty prevalence between different assessment methods. Use of EFS, frailty index and Fried phenotype (5 criteria, weakness and slowness not assessed using objective tests) were associated with a frailty prevalence approximately 20% higher than the reference method (Fried phenotype 5 criteria with objective tests). Geographic region was also a statistically significant predictor of frailty. The variables included in the model (mean age, % of females in the sample, study quality assessment score, geographic region and frailty assessment method) explained 54.9% of variability between the studies included in the analysis (table 1).

Table 1: Univariable and multivariable meta-regression results with all studies

Characteristic	Univariable analysis				Multivariable analysis			
	No of estimates	β (95% CI)	p value	Adjusted R^2 (%)	No of estimates	β (95% CI)	p value	Adjusted R^2 (%)
Mean age, years (per unit increase)	54	-0.006 (-0.025, 0.014)	0.558	-2.01	35	0.007 (-0.012, 0.027)	0.437	54.92
Percentage of females in the sample (per unit increase)	54	0.001 (-0.002, 0.005)	0.373	-0.62	35	0.000 (-0.004, 0.004)	0.997	
Study quality assessment score (per unit increase)	54	-0.014 (-0.049, 0.020)	0.411	-0.68	35	-0.008 (-0.041, 0.026)	0.648	
Geographic region *(Reference: South America)*	43			7.44	28			
Asia	9	-0.095 (-0.177,-0.014)	0.022		6	-0.093 (-0.174,- 0.013)	0.025	
Europe	2	0.044 (-0.117, 0.205)	0.584		1	0.109 (-0.064, 0.282)	0.206	
Frailty assessment method *(Reference: Frailty phenotype with 5 criteria, weakness and slowness assessed using objective tests)*	25			50.65	15			
Edmonton Frail Scale	5	0.217 (0.132, 0.303)	0.000		5	0.211 (0.118, 0.304)	0.000	
Frailty index	4	0.058 (-0.029, 0.145)	0.188		2	0.193 (0.067, 0.319)	0.004	
Fried phenotype with 4 criteria	13	0.037 (-0.019, 0.093)	0.187		12	0.045 (-0.029, 0.120)	0.222	
Fried phenotype with 5 criteria, weakness and slowness not assessed using objective tests	7	0.217 (0.147, 0.287)	0.000		1	0.277 (0.102, 0.451)	0.003	

DISCUSSION

Summary of main findings

No epidemiological studies on frailty were found from countries with low income economies ($ 1,045 or less) according to World Bank Classification, 2016[15]. Of countries with lower-middle-income economies ($ 1,046 to $ 4,125) we only found research in India as a study site of a multi-country study. All the other studies have been conducted in countries with upper-middle-income economies ($ 4,126 to $ 12, 735) indicating income inequality in frailty research.

The random effects pooled prevalence of frailty and pre-frailty in community dwelling older adults was 18.0% (95% CI= 15.0-22.0%) and 48.0% (95% CI= 45.0-51.0%) respectively. Frailty was significantly higher in females compared to males and as expected increased with age. This finding is consistent with previous research[12 23-26]. Interestingly, the prevalence of pre-frailty was stable across all age groups at around half the participants.

Comparison with existing literature

The prevalence of frailty and pre-frailty in middle income countries in this review was higher than the pooled prevalence in HICs reported previously (10.7% (95% CI= 10.5-10.9%) and 41.6% (95% CI= 41.2-42.0%) respectively[12]. However, it is also of note that the participants in HICs included people aged 65 years and above whereas 50% of studies in our meta-analysis included participants 60 years and above. Given that prevalence of frailty increases with age, when participants of a higher age group are selected, a higher prevalence would be expected. Our meta-analysis included 13 studies with a population aged 65 years and above. The prevalence of frailty of this sub sample was 14% (95% CI= 11.0-17.0%) and still higher compared to HICs. In the review of frailty in HICs, most studies were from Europe and North

America. A recent meta-analysis in Latin America and Caribbean only showed consistent finding to our study, with nearly one out of five older adult defined as frail[27].

We found lower prevalence rates when we restrict the meta-analysis only to the Fried phenotype with five criteria, including objective measures of weakness and slowness. This found a pooled prevalence of frailty of 12.0% and pre-frailty of 54.0%. This was still slightly higher than prevalence estimates for HICs similarly restricted to studies using Fried's phenotype criteria of 9.9% for frailty and 44.2% for pre-frailty[12]. Another review of the prevalence of frailty measured by the Fried phenotype based on community dwelling older adults above 65 years in national representative samples reported lower prevalence to our estimate except in the countries of Southern Europe (France, Italy, Greece, and Spain)[28]. Lower prevalence of frailty is also observed in high income Asian countries (Japan, Singapore and Taiwan) [26 29-31].

In contrast to these findings, a single multi-country study conducted with data from 14 high income countries in Europe and 6 low and middle income countries (China, Ghana, India, Mexico, Russian Federation and South Africa) reported higher frailty level (high mean frailty index) in high income countries compared to the low income countries[23]. They also found an inverse association between level of frailty and income and education in both high and low income countries. Individuals with poor education and low income were more likely to be frail. Higher levels of frailty in high income countries could be due to the higher survival rate of participants with advanced health care and social protection. On the other hand, as the frailty index is based on a list of deficits including diagnosed diseases, many medical conditions could be under reported/diagnosed in the participants in low income countries which could lead to lower levels of frailty defined using a cumulative deficit model.

In our study, even among the studies using Fried phenotype with objective criteria, there was considerable variation in operationalizing the five phenotypic criteria. Similarly the number of deficits used in frailty index and cut off points for defining frailty and pre-frailty status was inconsistent. Our review found significant differences in frailty prevalence according to the assessment method used. A further meta-analysis with all available studies including both higher and the lower and middle income countries would be valuable, controlling for frailty assessment method, sex and age composition of the sample. In addition methodologically comparable studies across countries are required to study the true population difference of frailty.

Strength and weaknesses

This is the first systematic review and meta-analysis on prevalence of frailty and pre-frailty among community dwelling older adults in LMICs. The strengths of our study include; we conducted a comprehensive literature search in six electronic databases with a comprehensive search strategy, including a regional database (LILACS) to capture studies published regionally, no language restriction, sub group analysis of prevalence of frailty and pre-frailty with substantial number of studies, and using a meta-regression technique to identify the sources of heterogeneity between the studies, contacting authors to get the additional information of the studies which required for sub group analyses. A limitation of this study was non-inclusion of grey literature.

Implications for practice

The findings of the study suggest that the prevalence of frailty appears higher among community dwelling older adults in middle income countries compared to high income countries. No studies were identified from low income countries and only one from a lower middle income country. Despite evidence that populations are rapidly ageing in many of

these countries, we do not currently know the prevalence of frailty in these populations to inform health and social care planning. Research is required from low and lower middle income countries with rapidly ageing populations to estimate burden of frailty and to understand how frailty affects the day-to-day lives of older people. Furthermore, a consensus is required on methods of assessing frailty to allow for more robust comparisons across populations.

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Competing interests

The authors declare that they have no competing interests.

Ethical Clearence

This study is a systematic review and meta-analysis using already published litearature. Hence, ethical approval is not required.

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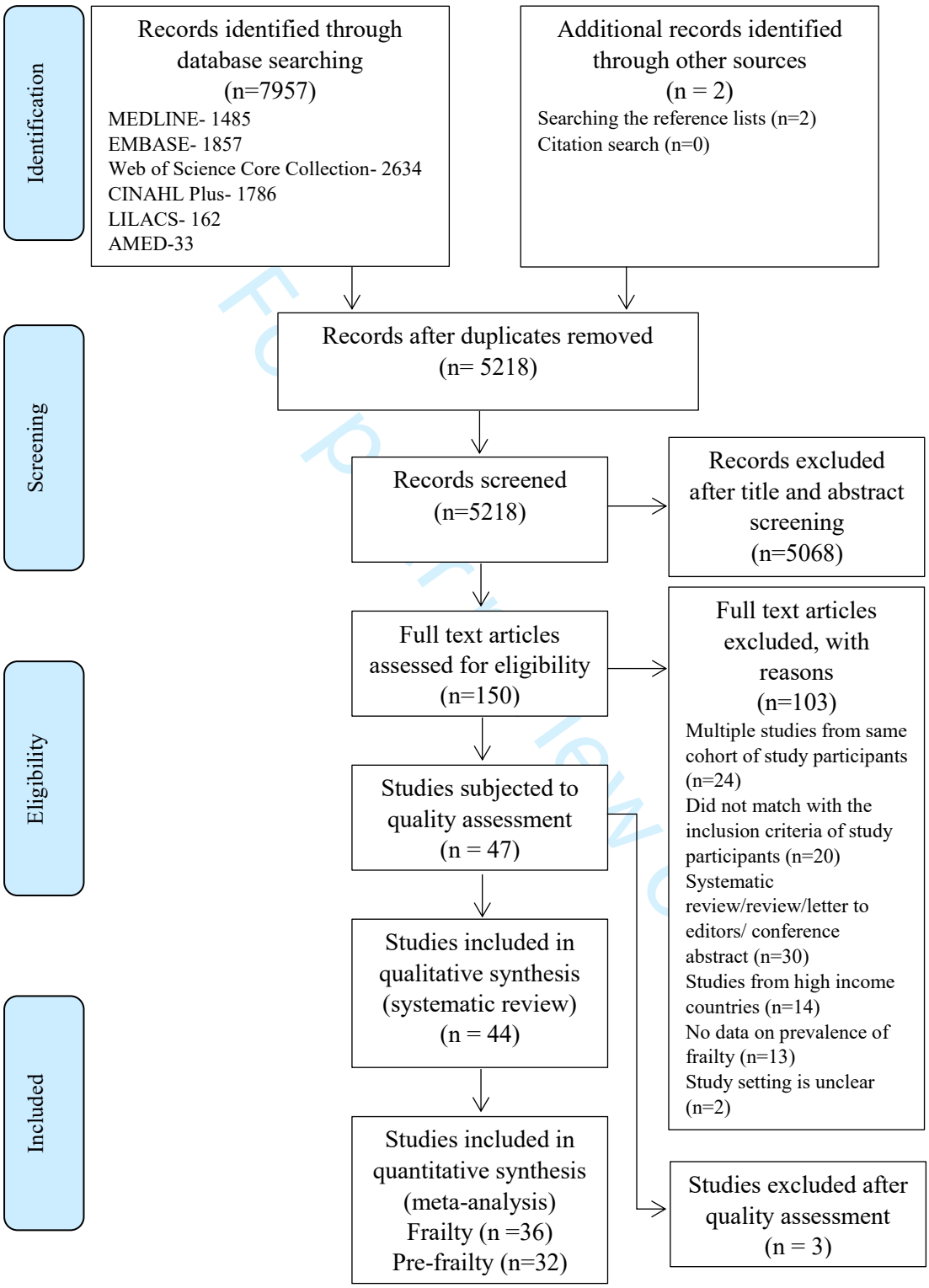
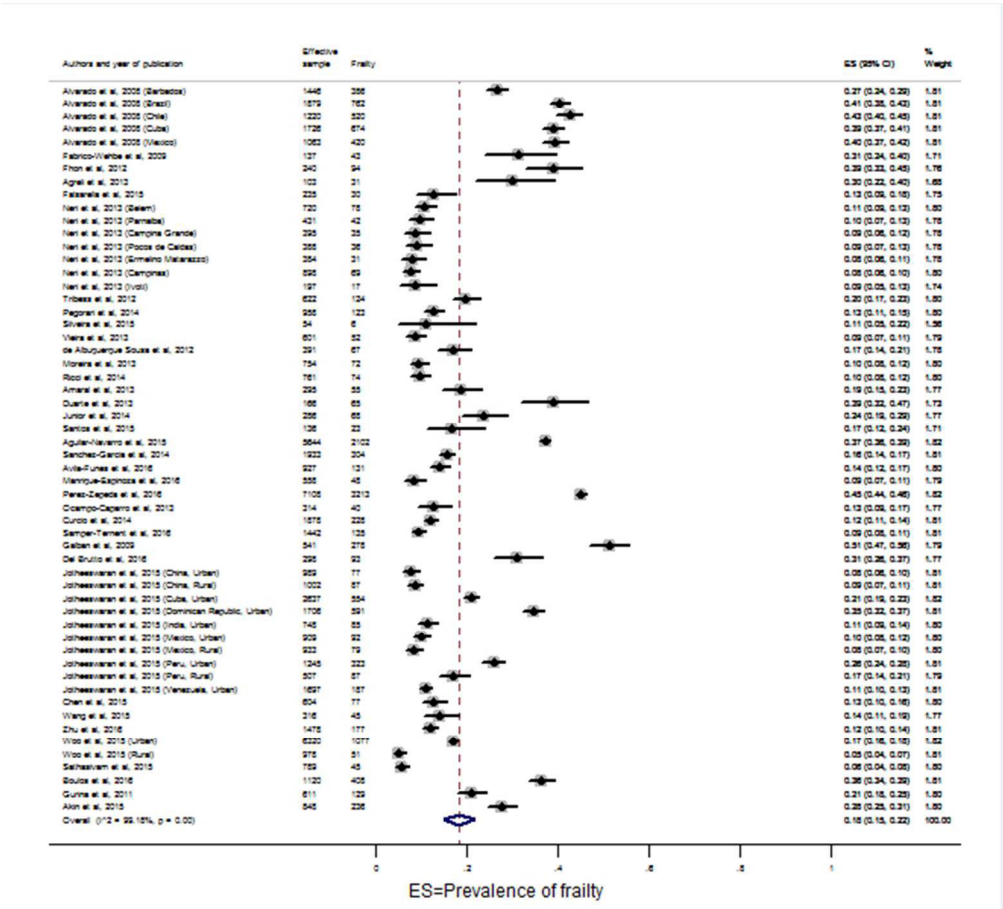
Contributors

Dhammika Deepani Siriwardhana (DDS), Kate Walters (KW) and Greta Rait (GR) conceived the idea of this systematic review. DDS designed, conducted the study and drafted the manuscript. Sarah Hardoon (SH) was the secondary reviewer of the systematic review and involved with screening, data extraction, study quality assessment, data analysis and provided important intellectual facts to revise the manuscript. KW, GR and Manuj Chrishantha Weerasinghe (MCW) provided important feedback at various stages of the study; devising the protocol, resolving the disagreements between DS and SH at the study selection process, clarifying the issues related to study quality assessment and interpreting the findings and providing important intellectual facts to revise the manuscript.

Data sharing statement

No additional data available.


Identification
Records identified through database searching (n=7957)
MEDLINE- 1485
EMBASE- 1857
Web of Science Core Collection- 2634
CINAHL Plus- 1786
LILACS- 162
AMED-33
Additional records identified through other sources (n = 2)
Searching the reference lists (n=2)
Citation search (n=0)
Screening
Records after duplicates removed (n= 5218)
Records screened (n=5218)
Records excluded after title and abstract screening (n=5068)
Eligibility
Full text articles assessed for eligibility (n=150)
Full text articles excluded, with reasons (n=103)
Multiple studies from same cohort of study participants (n=24)
Did not match with the inclusion criteria of study participants (n=20)
Systematic review/review/letter to editors/ conference abstract (n=30)
Studies from high income countries (n=14)
No data on prevalence of frailty (n=13)
Study setting is unclear (n=2)
Studies subjected to quality assessment (n = 47)
Studies included in qualitative synthesis (systematic review) (n = 44)
Included
Studies included in quantitative synthesis (meta-analysis)
Frailty (n =36)
Pre-frailty (n=32)
Studies excluded after quality assessment (n = 3)



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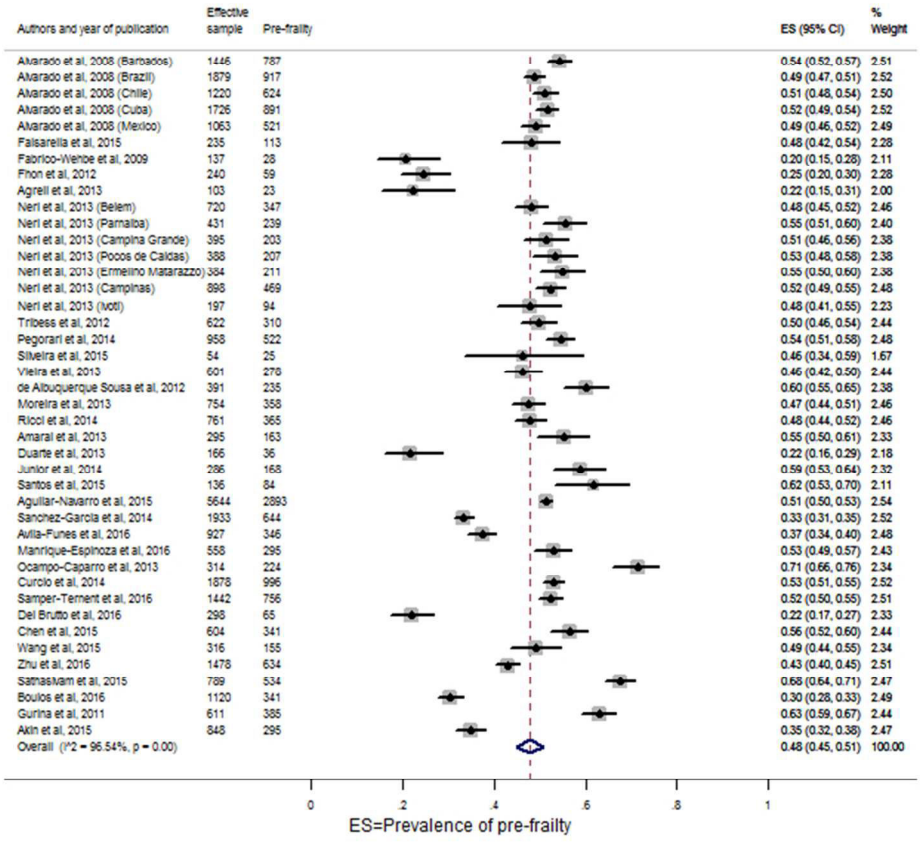


238x219mm (72 x 72 DPI)

Appendix A- MEDLINE Search Strategy

1. Frail Elderly.sh,kf.

2. (frail* or geriatric syndrome* or geriatric disorder*).ti,ab.

3. ((elder* or old* or senior* or geriatric*) adj4 function* adj4 (declin* or impair*)).af.

4. 1 or 2 or 3

5. Developing Countries.sh,kf.

6. (Africa* or Asia* or Caribbean* or West Indi* or South America* or Latin America* or Central America*).hw,kf,ti,ab,cp.

7. ((developing or less* developed or under developed or underdeveloped or middle income or low* income or underserved or under served or deprived or poor*) adj (countr* or nation? or population? or world)).ti,ab.

8. ((developing or less* developed or under developed or underdeveloped or middle income or low* income) adj (economy or economies)).ti,ab.

9. (low* adj (gdp or gnp or gni or gross domestic or gross national)).ti,ab.

10. (low adj3 middle adj3 countr*).ti,ab.

11. (lmic or lmics or third world or lami countr*).ti,ab.

12. transitional countr*.ti,ab.

13. (Afghanistan or Albania* or Algeria* or Angola* or Antigua or Barbuda or Argentin* or Armenia* or Aruba or Azerbaijan or Bahrain or Bangladesh* or Barbados or Benin or Byelarus or Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or Herzegovina or Hercegovina or Botswana or Brasil* or Brazil* or Bulgaria* or Burkina Faso or Burkina Fasso or Upper Volta or Burundi or Urundi or Cambodia* or Khmer Republic or Kampuchea or Cameroon or Cameroons or Cameron or Camerons or Cape Verde or Cabo Verde or Central African Republic or Chad or Chile or China or Chinese or Colombia* or Comoros or Comoro Islands or Comores or Mayotte or Congo or Zaire or Costa Rica or Cote d'Ivoire or Ivory Coast or Croatia or Cuba* or Cyprus or Czechoslovakia or Czech Republic or Slovakia or Slovak Republic or Djibouti or French Somaliland or Dominica or Dominican Republic or East Timor or East Timur or Timor Leste or Ecuador or Egypt* or United Arab Republic or El Salvador or Eritrea or Estonia* or Ethiopia* or Fiji or Gabon or Gabonese Republic or Gambia or Gaza or Georgia or Georgian or Ghana or Gold Coast or Greece or Grenada or Grenadines or Guatemala or Guinea or Guam or Guiana or Guyana or Haiti* or Honduras or Hungary or India* or Maldiv* or Indonesia* or Iran* or Iraq* or Isle of Man or Jamaica* or Jordan* or Kazakhstan or Kazakh or Kenya* or Kiribati or Korea* or Kosovo or Kyrgyzstan* or Kirghizia or Kyrgyz Republic or Kirghiz or Kirgizstan or Lao PDR or Laos or Latvia* or Lebanon or Lebanese or Lesotho or Basutoland or Liberia or Libya* or Lithuania* or Macedonia* or Madagascar or Malagasy Republic or Malaysia* or Malaya or Malay or Sabah or Sarawak or Malawi or Nyasaland or Mali or Malta or Marshall Islands or Mauritania or Mauritius or Agalega Islands or Mexic* or Micronesia or Middle East or Moldova or Moldovia or Moldovian or Mongolia* or Montenegro or Morocco or Ifni or Mozambique or Myanmar or Myanma or Burma or Namibia or Nepal* or Netherlands Antilles or New Caledonia or Nicaragua or Niger or Nigeria* or Northern Mariana Islands or Oman or Muscat or Pakistan or Palau or Palestine or Panama or Paraguay or Peru* or Philippines or Philipines or Phillipines or Phillippines or Poland or Portugal or Principe or Puerto Rico or Romania* or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or Saint Kitts or St Kitts or Nevis or Saint Lucia or St Lucia or Saint Vincent or St Vincent or Grenadines or Samoa* or Samoan Islands or Navigator Island or Navigator Islands or Sao Tome or Saudi Arabia or Senegal or Serbia* or Montenegro or Seychelles or Sierra Leone or Slovenia or Sri Lanka* or Ceylon or Solomon Islands or Somalia* or South Africa* or Sudan* or Suriname or Surinam or Swaziland or Syria or Tajikistan or Tadzhikistan or Tadjikistan or Tadzhik or Tanzania* or Thailand or Thai or Togo or Togolese Republic or Tonga or Trinidad or Tobago or Tunisia* or Turk* or Turkmenistan or Turkmen or Tuvalu or Uganda* or Ukrain* or Uruguay or USSR or Soviet Union or Union of Soviet Socialist Republics or Uzbekistan or Uzbek or Vanuatu or New

Hebrides or Venezuela or Vietnam* or Viet Nam* or West Bank or Yemen* or Yugoslavia or Zambia* or Zimbabwe* or Rhodesia*).hw,kf,ti,ab,cp.

14. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13

15. 4 and 14

Appendix B- Study Quality Assessment

Authors and year of publication*	Random sample or whole population	Unbiased sampling frame	Adequate sample size (>300 subjects)	Used standard measures	Outcomes measured by unbiased assessors	Adequate response rate (70%), refusers described	Confidence interval (CI) for prevalence, subgroup analysis	Study subjects are described	Risk of bias assessment
Alvarado et al, 2008[1]	√	√	√	√	×	√,×	×,√	√	6.0
De Andrade et al, 2013[2]	√	√	√	√	×	×,×	×,√	√	5.5
Corona et al, 2015[3]	√	√	√	√	√	√,×	×,√	√	7.0
Fabricio-Wehbe et al, 2009[4]	√	√	×	√	√	×,×	×,√	√	5.5
Fhon et al, 2012[5]	√	√	×	√	√	√,×	×,√	√	6.0
Agreli et al, 2013[6]	√	√	×	√	×	√,×	×,√	√	5.0
Falsarella et al, 2015[7]	√	×	×	√	×	√,×	×,×	√	3.5
Neri et al, 2013[8]	√	√	√	√	√	×,×	×,√	√	6.5
Tribess et al, 2012[9]	√	×	√	√	×	√,√	×,√	√	5.5
Pegorari et al, 2014[10]	√	×	√	√	√	√,√	×,√	√	6.5
Silveira et al, 2015[11]	√	√	×	√	×	×,×	×,×	√	4.0
Vieira et al, 2013[12]	√	√	√	√	×	×,√	×,×	√	5.5
de Albuquerque Sousa et al, 2012[13]	√	√	√	√	√	√,×	×,√	√	7.0
Moreira et al, 2013[14]	√	×	√	√	×	√,√	√,×	√	5.5
Ricci et al, 2014[15]	√	√	√	√	√	√,√	×,√	√	7.5
dos Santos Amaral et al, 2013[16]	×	×	√	√	√	√,×	×,×	√	4.5
Duarte et al, 2013[17]	√	×	×	√	×	√,×	×,×	√	3.5
Júnior et al, 2014[18]	√	N/A	×	√	×	√,√	×,√	√	4.5
Bastone et al, 2015[19]	×	×	×	√	×	√,√	×,×	√	3.0
Sampaio et al, 2015[20]	×	×	×	√	×	×,×	×,×	√	2.0
Santos et al, 2015[21]	×	×	×	√	√	√,×	×,√	√	4.0

Authors and year of publication*	Random sample or whole population	Unbiased sampling frame	Adequate sample size (>300 subjects)	Used standard measures	Outcomes measured by unbiased assessors	Adequate response rate (70%), refusers described	Confidence interval (CI) for prevalence, subgroup analysis	Study subjects are described	Risk of bias assessment
García-González et al, 2009[22]	√	√	√	√	√	×,×	×,√	√	6.5
Aguilar-Navarro et al, 2015[23]	√	√	√	√	√	×,×	×,√	√	6.5
de Leon Gonzalez, 2015[24]	√	×	√	√	×	×,×	×,√	√	4.5
Garcia-Pena et al, 2016[25]	√	√	√	√	√	√,√	×,√	√	7.5
Sanchez-Garcia et al, 2014[26]	√	√	√	√	√	N/A	×,√	√	6.5
Avila-Funes et al, 2016[27]	√	√	√	√	√	√,√	×,√	√	7.5
Manrique-Espinoza et al, 2016[28]	√	√	√	√	×	√,√	×,√	√	6.5
Perez-Zepeda et al, 2016[29]	√	√	√	√	√	√,×	×,×	√	6.5
Ocampo-Chaparro et al, 2013[30]	√	√	√	√	√	√,×	×,√	√	7.0
Curcio et al, 2014[31]	×	×	√	√	√	×,×	×,√	√	4.5
Samper-Ternent et al, 2016[32]	√	×	√	√	√	×,√	×,√	√	6.0
Rosero-Bixby et al, 2009[33]	√	√	√	√	√	×,√	×,√	√	7.0
Galban et al, 2009[34]	×	×	√	√	×	√,×	×,√	√	4.0
Del Brutto et al, 2016[35]	√	N/A	√	√	×	√,√	×,√	√	5.5
Jotheeswaran et al, 2015[36]	√	N/A	√	√	√	√,×	×,×	√	5.5
Chen et al, 2015[37]	×	×	√	√	√	×,√	×,√	√	5.0
Wang et al, 2015[38]	×	×	√	√	√	×, ×	×,√	√	4.5
Zhu et al, 2016[39]	√	√	√	√	√	√, √	×, ×	√	7.0
Bennett et al, 2013[40]	×	×	√	√	√	×, ×	×,√	√	4.5
Woo et al, 2015[41]	√	√	√	√	√	×, ×	×,√	√	6.5
Hao et al, 2016[42]	√	√	√	√	√	×, ×	√,√	√	7.0
Sathasivam et al, 2015[43]	√	√	√	√	×	√,×	×,√	√	6.0

Authors and year of publication*	Random sample or whole population	Unbiased sampling frame	Adequate sample size (>300 subjects)	Used standard measures	Outcomes measured by unbiased assessors	Adequate response rate (70%), refusers described	Confidence interval (CI) for prevalence, subgroup analysis	Study subjects are described	Risk of bias assessment
Boulos et al, 2016 [44]	√	√	√	√	√	√,×	×,√	√	7.0
Gurina et al, 2011 [45]	√	√	√	√	√	×,√	×,√	√	7.0
Akin et al, 2015 [46]	√	√	√	√	×	×, ×	×,√	√	5.5
Cakmur et al, 2015 [47]	×	×	×	√	×	√,×	×, ×	√	2.5

√- Criteria is satisfied ×- Criteria is not satisfied/ not documented N/A- Not applicable

Appendix C: Characteristics of the studies included in the systematic review and prevalence of frailty and pre-frailty

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants' mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI pre-frailty	Prevalence (%), 95% CI frailty	Study strengths reported by authors	Study limitations reported by authors
Alvarado et al, 2008[1]	Barbados Brazil Chile Cuba Mexico	Health, Wellbeing and Ageing study (SABE) study Conducted in 1999-2000	Multi centric cross sectional study	7334	-	≥ 60	Multi-staged sampling	Fried phenotype §	-	-	-	Operationalization of Fried phenotypic criteria is different from the original Cardiovascular Health Study (CHS) of Fried et al, 2001. And also, possible background risk differences (cultural and other social biological factors) may limit the comparison of this study results with other studies.
		Bridgetown, Barbados		1446	61.1				54.4	26.7		
		São Paulo, Brazil		1879	59.3				48.8	40.6		
		Santiago de Chile, Chile		1220	66.1				51.4	42.6		
		Havana, Cuba		1726	62.7				51.6	39.0		
		Mexico, DC, Mexico		1063	60.4				49.0	39.5		
De Andrade et al, 2013[2]	Brazil	SABE study (Wave 2-2006) Survivors from baseline study (2000) and new participants of the second wave São Paulo	Cross sectional study with SABE data	1374	59.7	≥ 60	Cluster sampling	Fried Phenotype ǂ	40.7	8.5	Use of large representative sample of community dwelling elderly increases the generalizability of results. Frailty has measured using well defined method.	Use of self-reported data regarding physical activities may introduce biases that are difficult to control.
Corona et al, 2015[3]	Brazil	SABE study (Wave 3-2010), Survivors from baseline (2000) and second wave (2006) and new participants of the third wave São Paulo	Cross sectional population based study	1256	60.9	≥ 60	Probabilistic sampling	Fried Phenotype ǂ	50.3	8.0	Large population base cohort, with a representative sample of community dwelling older adults from the largest city in Brazil.	-
Fabricio-Wehbe et al, 2009[4]	Brazil	Ribeirao Preto, Sao Paulo September 2007-June 2008	-	137	74.5	≥ 65 (75.3±8.0) 65-100	Probabilistic sampling	Edmonton frail scale	20.4	31.4	-	-

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants'/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									pre-frailty	frailty		
Fhon et al, 2012[5]	Brazil	Municipality of Ribeirao Preto, Sao Paulo Conducted in November 2010-February 2011	Cross sectional study	240	62.9	≥ 60 (73.5±8.4)	Two stage conglomerate sampling	Edmonton frail scale	24.6	39.2	-	-
Agreli et al, 2013[6]	Brazil	Embu, City in metropolitan region of Sao Paulo Conducted in June-July 2010	Observational descriptive cross sectional study	103	62.1	≥ 60 (68.9±7.8) 60-103	Simple random sampling	Edmonton frail scale	22.3	30.1	-	Older adults who did not respond to the clock test could not classify for their degree of frailty.
Falsarella et al, 2015[7]	Brazil	Urban area of the municipality of Amparo, State of Sao Paulo	Cross sectional study	235	60.4	≥ 65 (71.7±5.0)	Random sampling	Fried Phenotype ǂ	48.0	12.7	-	Small sample size. Has excluded most sick and debilitated older adults.
Neri et al, 2013[8]	Brazil	FIBRA Seven cities	Cross sectional study	3413	67.6	≥ 65	Probability sampling	Fried Phenotype ǂ	51.9	9.0	Measures were taken to avoid the systematic distortions of data. i.e. encouraging participation of the elderly, standardization of procedures, instruments and equipment, comprehensive training of staff in all locations, procedures were adopted to ensure greater reliability of data entered in the electronic banks.	More female representation in the study sample limited the generalizability of results. Loss of information during the data collection was a limitation of the reliability of data. Loss of participants in Ivoti where the sample is lower than the expected due to refusal to attend data collection because of the problems of time and transport. Selection of older people without cognitive
		Belem		720	69.5				48.2	10.8		
		Parnaiba		431					55.5	9.7		
		Campina Grande		395	70.1	73.9			51.4	8.9		
		Pocos de Caldas		388	61.4				53.4	9.3		
		Ermelino Matarazzo, Sao Paulo		384	67.2				54.9	8.1		
		Campinas		898	69.3				52.2	7.7		
		Ivoti		197	70.1				47.7	8.6		

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									pre-frailty	frailty		
Neri et al, 2013[8] cont.												impairment and required to attend to the data collection site by their own might introduced the survival bias into the study.
Tribess et al, 2012[9]	Brazil	Population Study of Physical Activity and Aging (EPAFE), City of Uberaba, Minas Gerais Conducted in May-August 2010	Cross sectional study	622	65	≥ 60 (71.0±7.7) 60-96	Random sampling	Fried Phenotype ǂ	49.8	19.9	Socio-demographic characteristics of the elderly in this study are similar to those reported in surveys in Latin America indicates the potential generalization of the present results to other populations.	The measurements of self-perception may have been influenced by the low educational level of participants and their motivational aspects.
Pegorari et al, 2014[10]	Brazil	Urban area of the city of Uberaba, MG	Cross sectional observational and analytical household survey	958	64.4	≥ 60 (73.7±6.7)	Stratified proportional sampling	Fried Phenotype ǂ	54.5	12.8	Results of the study contribute to deepen knowledge of frailty syndrome among Brazilian elderly individuals and support planning and implementation of interventions and care actions.	-
Silveira et al, 2015[11]	Brazil	Uberaba, Minas Gerais July-October 2011	Analytical observational cross sectional study	54	59.3	≥ 65 (72.9±6.0)	Random sampling	Fried Phenotype ǂ	46.2	11.1	-	-
Vieira et al, 2013[12]	Brazil	FIBRA-Belo Horizonte, Minas Gerais State December 2008-September 2009	Population based cross sectional study	601	66.2	≥ 65 (74.3±6.4)	Probability sampling	Fried Phenotype ǂ	46.3	8.7	-	Phenotype limits the evaluation of possible frail elderly with cognitive impairment, gait

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI pre-frailty	Prevalence (%), 95% CI frailty	Study strengths reported by authors	Study limitations reported by authors
Vieira et al, 2013[12] cont.												restriction, severe motor sequale. Use of Minnesota Questionnaire of Physical Activities and Leisure is not fitting with the Brazilian cultural context.
de Albuquerque Sousa et al, 2012[13]	Brazil	FIBRA- urban zone of Santa Cruz city	Cross sectional study	391	61.4	≥ 65 (74.0±6.5) 65-96	Random sampling	Fried Phenotype ǂ	60.1	17.1	-	Adapted version of the Minnesota Questionnaire of Physical Activities and Leisure was used in this study as original questionnaire did not match with Brazilian cultural context. The used cut-off point (20th percentile) may be underestimating the physical activity level.
Moreira et al, 2013[14]	Brazil	FIBRA- Northern area of the city of Rio de Janeiro Conducted in January 2009-January 2010	Cross sectional descriptive study	754	66.9	≥ 65 (76.6±6.9)	Inverse random sampling stratified by gender and age	Fried Phenotype ǂ	47.3 (43.8-50.8)	9.1 (7.3-11.3)	-	An adapted version of Minnesota Questionnaire of Physical Activities and Leisure was used in this study. However, it is also problematic as reference activities in the questionnaire are atypical in Brazilian culture. This may lead to errors in estimating the weekly caloric expenditure.

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									pre-frailty	frailty		
Ricci et al, 2014[15]	Brazil	FIBRA- Barueri and Cuiaba urban municipalities	Cross sectional population based study	761	64.3	≥ 65 (71.9±5.9)	Census of older adults in 27 census tracts	Fried Phenotype ǂ	48.0	9.7	-	The phenotype used in the study basically comprised of physical frailty and not include other markers such as cognitive decline and psychosocial aspects.
dos Santos Amaral et al, 2013[16]	Brazil	This study is a part of a project titled "Allostatic load, frailty and functionality in the elderly" Neighbourhood Rocas, Natal	Analytical observational cross sectional study	295	67.3	≥ 65 (74.3±6.9) 65-100	-	Fried Phenotype ǂ	55.3	18.6	Representativeness of the sample. Low percentage of refusals.	-
Duarte et al, 2013[17]	Brazil	This study is a sub project of the survey "Living conditions, health and ageing: a comparative study" City of Joao Pessoa, the state capital of Paraiba April-June 2011	Cross sectional study	166	100.0	≥ 60 (73.0±6) 60-96	Two staged cluster sampling	Edmonton frail scale	21.7	39.2	-	-
Júnior et al, 2014[18]	Brazil	Epidemiological study titled Nutritional status, risk behaviours and health conditions of the elderly people of Lafaiete Coutinho-BA Urban area	Cross sectional study	286	54.2	≥ 60	Census of all older adults in the area	Fried Phenotype ǂ	58.7	23.8	-	Some instruments used in the study required subjective or self-reported information that can be lead to memory bias.

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI pre-frailty	Prevalence (%), 95% CI frailty	Study strengths reported by authors	Study limitations reported by authors
Santos et al, 2015[21]	Brazil	Database called "Identifying the health disease process enrolled population at the Family Health Units" Pau Ferro, municipality of Jequie/BA May-November 2013	Observational cross sectional study	136	75.5	≥60 (72.3±8.4) 60-101	-	Fried Phenotype ǂ	61.8	16.9	-	-
García-González et al, 2009[22]	Mexico	Mexican health and Aging Study (MHAS) Wave 1	Follow up study	4082	52.5	≥65 (73.0)	Probabilistic sample	Frailty index (FI) -34 variables	5 FI levels .00-.07-17.4 .07-.14-30.8 .14-.21-24.0 .21-.35-21.4 .35-.65-6.5		-	-
Aguilar-Navarro et al, 2015[23]	Mexico	Subset from Mexican health and Aging Study (MHAS) Wave 1 Conducted in summer of 2001	Longitudinal study (cross sectional data)	5644	53.6	≥ 60 (68.7±6.9)	Random sample	Fried Phenotype §	51.3	37.2	Population based design. Sample size	Operationalization of Fried phenotypic criteria is different from the original CHS of Fried et al, 2001. The original metrics were not available in the MHAS cohort. It could results possible overestimation of prevalence of frailty.
de Leon Gonzalez, 2015[24]	Mexico	Mexican Health and Aging Study (MHAS) Wave 1		4729	-	≥60	-	FRAIL scale	44.8	10.4	Large sample size of men and women living in the community.	Subjects who do not complete the performance measures in population studies, and not included in the present analysis are expected to be less healthy and more likely to die.

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									pre-frailty	frailty		
de Leon Gonzalez, 2015[24] cont.												This increases the possibility of survival bias.
Garcia-Pena et al, 2016[25]	Mexico	Mexican health and Aging Study (MHAS) Wave 3 Conducted in 2012	Secondary analysis	1108	54.6	≥ 60 (69.8±7.6)	-	Fried Phenotype ǂ Frailty index-32 variables	- -	24.9 27.5	Large comprehensive dataset. Used previously validated frailty classifying tools (Fried phenotype and frailty index)	The cut-off value to define frailty by frailty index was arbitrary although it was based on previous research. Included 32 deficits in frailty index as self-rated hearing and abdominal pain were not available in the 2012 wave. Categorization of physical activity in Fried phenotype was different from previous reports.
Sanchez-Garcia et al, 2014[26]	Mexico	Data from Study on Aging and Dementia in Mexico (SADEM) Conducted in September 2009-March 2010	Not mentioned in the article	1933	58.0	≥ 60 70.1±7.1 (women) 71.7±7.4 (men)	Random sample from original database	Fried Phenotype with 4 criteria	33.3	15.7	-	Definitions used to evaluate frailty and pre-frailty.
Avila-Funes et al, 2016[27]	Mexico	Subset of Mexican Study of Nutritional and Psychosocial Markers of Frailty (prospective cohort study) Coyoacán cohort Conducted in April 2008-July 2009	Cross-sectional study using the data of prospective cohort study	927	54.9	≥ 70 Median age-76.5 70.3-104.4	Random sampling stratified by age and sex	Fried Phenotype §	37.3	14.1	Population based sample, from a cohort specifically designed to identify the Correlates of frailty.	Recruitment was carried out in only one district of Mexico city, therefore these results might not be representative of rural areas of Mexico.

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									pre-frailty	frailty		
Manrique-Espinoza et al, 2016[28]	Mexico	Impact evaluation study conducted in 516 rural localities 2009	Cross sectional study	558	47.5	≥70	Simple random sampling	Fried Phenotype ǂ	52.9	8.6	Used objective frailty measure (Fried phenotype) which allowed to produce reliable and precise findings comparable with those other studies.	Though the non-response rate low as 7%, excluded elderly were mostly illiterate, with greater ADL and IADL disability and greater prevalence of depressive symptoms. Along with the presence of poorer health, higher prevalence of frailty can be assumed.
Perez-Zepeda et al, 2016[29]	Mexico	Data from nationwide survey representing urban and rural areas,"Mexican Survey on Nutrition and Health (ENSANUT), 2012	Cross sectional analysis	7108	54.7	≥ 60 70.7±8.1	Multistage stratified sampling	Frailty index-44 variables	-	45.2	-	-
Ocampo-Chaparro et al, 2013[30]	Colombia	Commune 18, City of Cali (urban area) Conducted in 2009	Population based cross sectional study	314	64.3	≥ 60	Single stage cluster sampling	Fried Phenotype ǂ	71.3	12.7	-	The study was conducted in a localized area and not in the entire city of Cali. And also study population did not include rural, institutionalized adults. Hence it limited the external validity of the findings

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									pre-frailty	frailty		
Curcio et al, 2014[31]	Colombia	Four villages located in the coffee growing zone of the Andese mountains, (rural area) Conducted in 2005	Cross sectional study	1878	52.2	≥ 60 (70.9±7.4)	Voluntary participation	Fried Phenotype ǂ	53.0	12.2	Number of participants. Used comprehensive set of measurements and the setting of the assessment. Measured the prevalence of frailty in older adults living in rural areas in the Latin American Countries. Established the relationship Between frailty, higher prevalence of chronic conditions and disabilities among elderly people in Latin America.	-
Samper-Ternent et al, 2016[32]	Colombia	Data from Salud Bienestar y Enve-Jecimiento (SABE) Bogota study Both urban and rural areas of Bogota Data collected in 2012	Cross sectional survey	1442	61.0	≥ 60 (70.7±7.7)	Probabilistic sampling by clusters with block stratification	Fried Phenotype ǂ	52.4	9.4	First population based study of adults over 60 in Colombia to explore conditions that affect their health and quality of study. Study followed the international guidelines previously used in other capital cities in Latin America and was modified to fit the social and historical situation of	Modification to the frailty phenotype definition could introduce bias to our analysis. Large percentage of cohort from the current study as there was missing data for construction of frailty and sarcopenia variables (n=558). Excluded individuals were significantly

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									pre-frailty	frailty		
Samper-Ternent et al, 2016[32]											Colombia. Used constructs validated in similar populations for assessed frailty previously.	different from study population which introduce bias to the study. Some data are self-reported so recall bias could. affect the results.
Rosero-Bixby et al, 2009[33]	Costa-Rica	Costa Rican Study on Longevity and Healthy Aging (CRELES)	-	2704	-	≥ 60	Random sampling	Physical frailty using five physical tests	- -	17.8 (60-79 years 57.0 (80+ years)	-	-
Galban et al, 2009[34]	Cuba	Antonio Maceo, Cerro municipality, Havana, Cuba Data collected in 2005	Observational descriptive cross sectional study	541	58.0	≥ 60	-	Geriatric Functional Assessment Scale was applied classified to frail and non-frail groups according to Cuban frailty criteria	-	51.4	-	-
Del Brutto et al, 2016[35]	Ecuador	Atahualpa, a rural village of costal Ecuador	Cross sectional population based study	298	57.0	≥ 60 (70.0±8.0)	Individuals identified through yearly door-to-door survey	Edmonton frail scale	22.0	31.2	Population based design. Lack of selection bias. Used a reliable instrument to identify frailty.	-
Jotheeswaran et al, 2015[36]	China Mexico Peru Cuba Dominican Republic Venezuela India	10/66 Dementia Research Group's (10/66 DRG) population based studies of ageing and dementia in LMICs Data collected between 2003 and 2007	Cross sectional survey	12373	62.3	≥ 65 (74.1±7.0)	Census	Fried Phenotype with 4 criteria Multi dimentional frailty model	- -	17.5 29.1	Study was conducted with large population based cohorts in Latin America, India and China allowing to assess the consistency or cultural specificity of the observed	Hand grip strength was not measured in this study. Hence physical frailty construct is only an approximation to the original Fried definition. The impact of this

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									pre-frailty	frailty		
Jotheeswaran et al, 2015[36] cont.		China (Urban)		989	56.6	(74.1±6.3)		Fried Phenotype with 4 criteria	-	7.8	associations.	omission is difficult to assess.
		China (Rural)		1002	55.5	(72.4±6.0)			-	8.7	Study design was prospective, limiting information bias with modest attrition.	
		Cuba (Urban)		2637	65.0	(75.2±7.1)			-	21.0		
		Dominican Republic (Urban)		1706	66.3	(75.4±7.6)			-	34.6		
		India (Urban)		748	57.2	(71.4±6.1)			-	11.4		
		Mexico (Urban)		909	66.5	(74.4±6.6)			-	10.1	Walking speed, under nutrition and cognitive impairment were measured objectively.	
		Mexico (Rural)		933	60.9	(74.1±6.6)			-	8.5		
		Peru (Urban)		1245	64.7	(75.0±7.4)			-	25.9		
		Peru (Rural)		507	53.2	(74.1±7.3)			-	17.2		
		Venezuela (Urban)		1697	63.2	(72.3±6.8)			-	11.0		
		China (Urban)		989	56.6	(74.1±6.3)		Multi dimentional frailty model	-	11.3	Visual and auditory impairment have been assessed by objective testing.	
		China (Rural)		1002	55.5	(72.4±6.0)			-	22.5		
		Cuba (Urban)		2637	65.0	(75.2±7.1)			-	33.7		
		Dominican Republic (Urban)		1706	66.3	(75.4±7.6)			-	47.8		
		India (Urban)		748	57.2	(71.4±6.1)			-	26.1		
		Mexico (Urban)		909	66.5	(74.4±6.6)			-	22.9		
		Mexico (Rural)		933	60.9	(74.1±6.6)			-	36.2		
		Peru (Urban)		1245	64.7	(75.0±7.4)			-	28.2		
		Peru (Rural)		507	53.2	(74.1±7.3)			-	25.6		
		Venezuela (Urban)		1697	63.2	(72.3±6.8)			-	20.0		
Chen et al, 2015[37]	China	Data from a cross sectional study, Comprehensive Geriatric Assessment and Health Care Service Study	Cross sectional study	604	57.9	≥ 60 (70.6±6.8) 60-91	Convenience sampling	Fried Phenotype ǂ	56.5	12.7	-	Data must be interpreted with caution. The number of the participants was below 1000, although the study

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI pre-frailty	Prevalence (%), 95% CI frailty	Study strengths reported by authors	Study limitations reported by authors
Chen et al, 2015[37] cont.	China	Chengdu and Suining, Southwest China Conducted in October 2010-August 2012										population was representative of the 60+ year old community dwelling adults in this specific area. The information about disease and some of the frailty items measurements were taken through self-reported questionnaires. Older people who refused to participate had lower level of functionality which might have nonresponse bias or selection bias. Present study only included Han people. Therefore, conclusions might not generalizable to other ethnic populations.
Wang et al, 2015[38]	China	Changsha city and its surrounding area Conducted in August 2012-August 2014	-	316	48.1	≥ 65 (75.6±4.8) (men) (76.9±5.2) (women)	-	Fried Phenotype ǂ	49.1	14.2	Participants were recruited from a community based elderly population.	Individuals were originally excluded if unable to walk without assistance of another person, or their renal function and liver function is abnormal, or their heart function classification is

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI pre-frailty	Prevalence (%), 95% CI frailty	Study strengths reported by authors	Study limitations reported by authors
Wang et al, 2015[38] cont.												grades III and IV according to New York Heart Association standard. This may have biased the results towards an underestimation of the risk of frailty associated with sarcoosteopenia
Zhu et al, 2016[39]	China	Cross sectional data from the ageing arm of the Rugao Longevity and Ageing Study 31 villages in Jiang'an township, Rugao city Conducted November 2014-December 2014	-	1478	53.0	≥ 70 75.3±3.9 (70-84)	Random sampling	Frailty phenotype with 4 criteria	42.9	12.0	Representativeness of the study participants increases the generalisabality of the findings. The study participants were randomly selected with a higher participant rate (91.2%) representing approximately 16% of the elderly in Jiang'an township. The Findings from such a representative population based sample might be generalisable to most elderly people in China.	-
Bennett et al, 2013[40]	China	Longevity Study (CLHLS) 22 provinces of China	Secondary analysis	6300	-	80-99	-	Frailty Index 38 deficits	FI≤ 0.05-15.0 0.05< FI≤ 0.15-53.2 0.15< FI≤ 0.25-20.2 0.25< FI≤ 0.35-		-	The baseline cohort included 36% centenarians and they have been excluded from the analysis. Hence,

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI pre-frailty	Prevalence (%), 95% CI frailty	Study strengths reported by authors	Study limitations reported by authors
Bennett et al, 2013[40] cont.									6.7 0.35< FI≤ 0.45-3.3 FI >0.45-1.6			results should be interpreted with caution.
Woo et al, 2015[41]	China	Data from Beijing Longitudinal Study of Aging II (BLSA II) Three urban districts (Xuanwu, Xicheng and Dongcheng) and one rural county (Shunyi) from the 18 administrative districts or counties in Beijing Participants recruited from July to November 2009	-	6320 (urban) 978 (rural)	61.5 57.2	≥ 65 74.6±5.6 (men) 73.8±5.2 (women) (74.8±5.7) (men) (73.9±5.0) (women)	Multistage cluster sampling	Frailty Index 34 variables	- -	17.0 5.2	-	-
Hao et al, 2016[42]	China	Data from Project of Longevity and Aging in Dujiangyan Dujiangyan region, Sichuan province	Cross sectional study	767	68.0	≥ 90 (93.7±3.4) 90-108	Based on a census of older people above 90 years	Frailty Index 35 variables	-	61.8	Frailty index does not rely on specific set of variables. Hence evaluation of frailty is more feasible.	Data needed to be interpreted with caution. The number of participants who gave the consent is still limited. The study population clearly represent a survivor group.
Sathasivam et al, 2015[43]	Malaysia	Urban district	Multistage cross sectional study	789	59.4	≥ 60 (69.6±7.2)	Multi stage random sampling	Frailty Index 40 variables	67.7	5.7	Population based study.	Use of appropriate cut-off values to depict the severity of frailty levels in the study population as there are no normative values that have been consensually

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI pre-frailty	Prevalence (%), 95% CI frailty	Study strengths reported by authors	Study limitations reported by authors
Sathasivam et al, 2015[43] cont.												established to date to define frailty in Malaysia. Findings cannot be generalised to other ethnic groups from similar middle income countries.
Boulos et al, 2016[44]	Lebanon	Rural areas Conducted in March 2011-2012	Cross sectional study	1120	50.8	≥ 65 (75.7±7.1)	Multi staged cluster sampling	Study of Osteoporotic Fractures (SOF) frailty index	30.4	36.4	Results may be generalisable to rural Lebanese elderly as study involved large representative sample with high response rate. This is the first study reporting estimates about frailty and associated factors in elderly Lebanese community dwellers. Data collection for frailty was based on a widely used and well validated instrument.	First part of questionnaire was based on self-reported information which might be affected by memory and education bias due to educational disparities. Cognitive impairment might affect the accuracy of the SOF index and underestimate the frailty. Widely used Fried phenotype was not used in this study due to the difficulty of performing the walking test (possible space constraints and lack of standardized conditions in Lebanese rural households.)

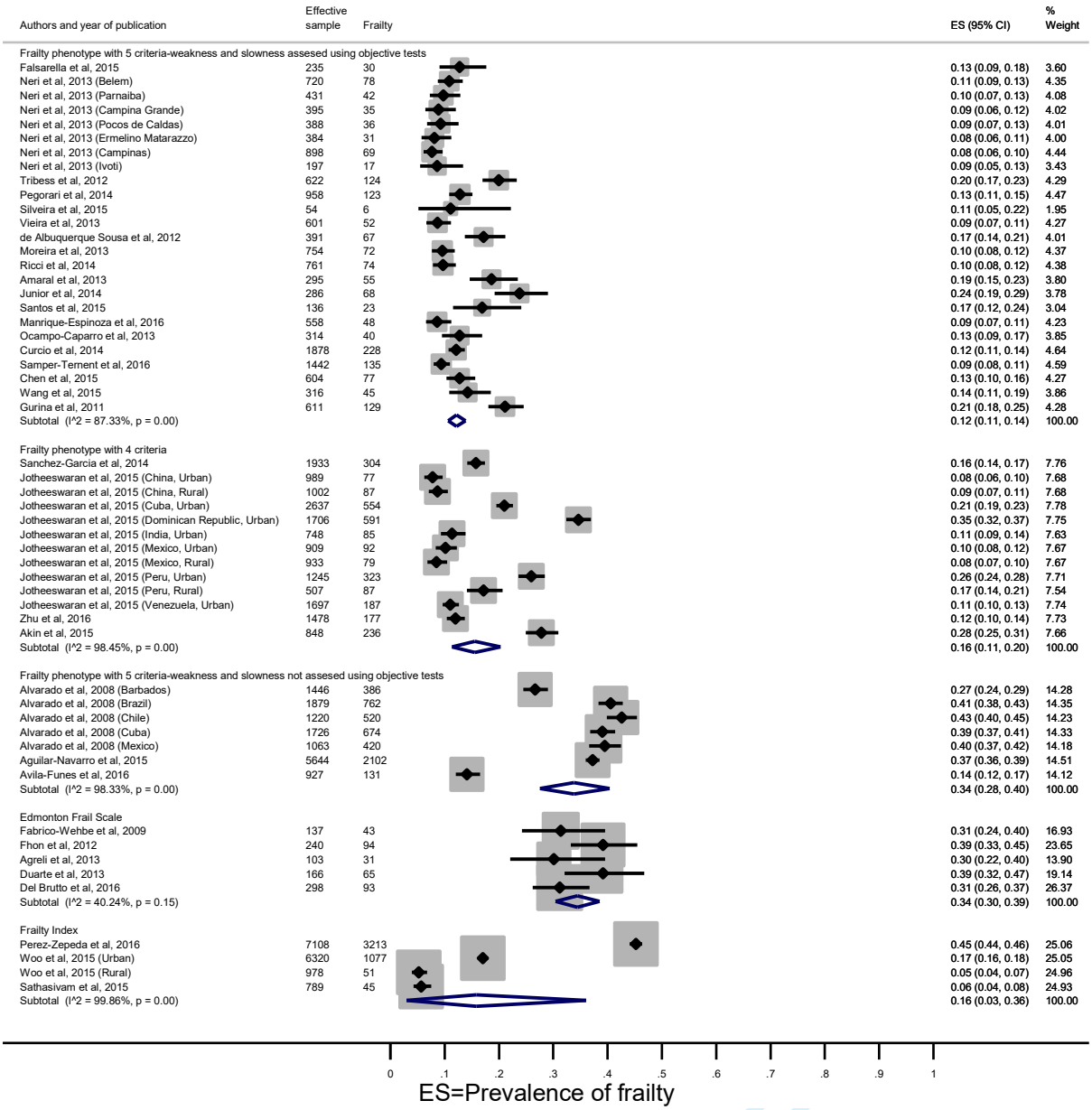
Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI pre-frailty	Prevalence (%), 95% CI frailty	Study strengths reported by authors	Study limitations reported by authors
Gurina et al, 2011[45]	Russia	Data from "Crystal" prospective cohort study Kolpino district of St. Petersburg Conducted March-December 2009	Cross sectional study	611	71.7	≥ 65 (75.1±5.9)	Random sample stratified by age	Fried Phenotype ǂ (whole study population) Fried Phenotype ǂ (adjusted for MMSE score <18, Parkinson's disease, and stroke) Steverink–Slaets model, Groningen Frailty Indicator Extended Puts model	63.0 65.5 24.7 42.9	21.1 17.9 32.6 43.9	Analysis provides a better understanding of the health status of older adults in Russia.	Cross sectional analysis is not adequate for frailty analysis as this phenotype is more dynamic than static. The prognostic significance of the different frailty indicators and models will become clearer after the follow up data are analysed. The tested frailty models were modified by using proxies for some of the original indicators. Findings can be generalized to the whole population of St. Petersburg only with caution, the Kolpino district represents one of the 18 districts of the city.
Akin et al, 2015[46]	Turkey	Kayseri (urban area) Data of Kayseri Elderly Health Study (KEHES) Kayseri Conducted in August-December 2013	Cross sectional population based study	848 897	50.6	≥ 60 (71.5±5.6)	Stratified random sampling and any Individual older than 60 years who requested to participate was also included.	Fried Phenotype with 4 criteria FRAIL scale	34.8 45.6	27.8 10.0		Absence of physical activity in our study may have under or overestimate the prevalence of frailty. The relatively small sample size of elderly subjects in ≥ 85 years.

Fried Phenotype ǂ = Fried Phenotype with 5 criteria-weakness and slowness assessed using objective tests

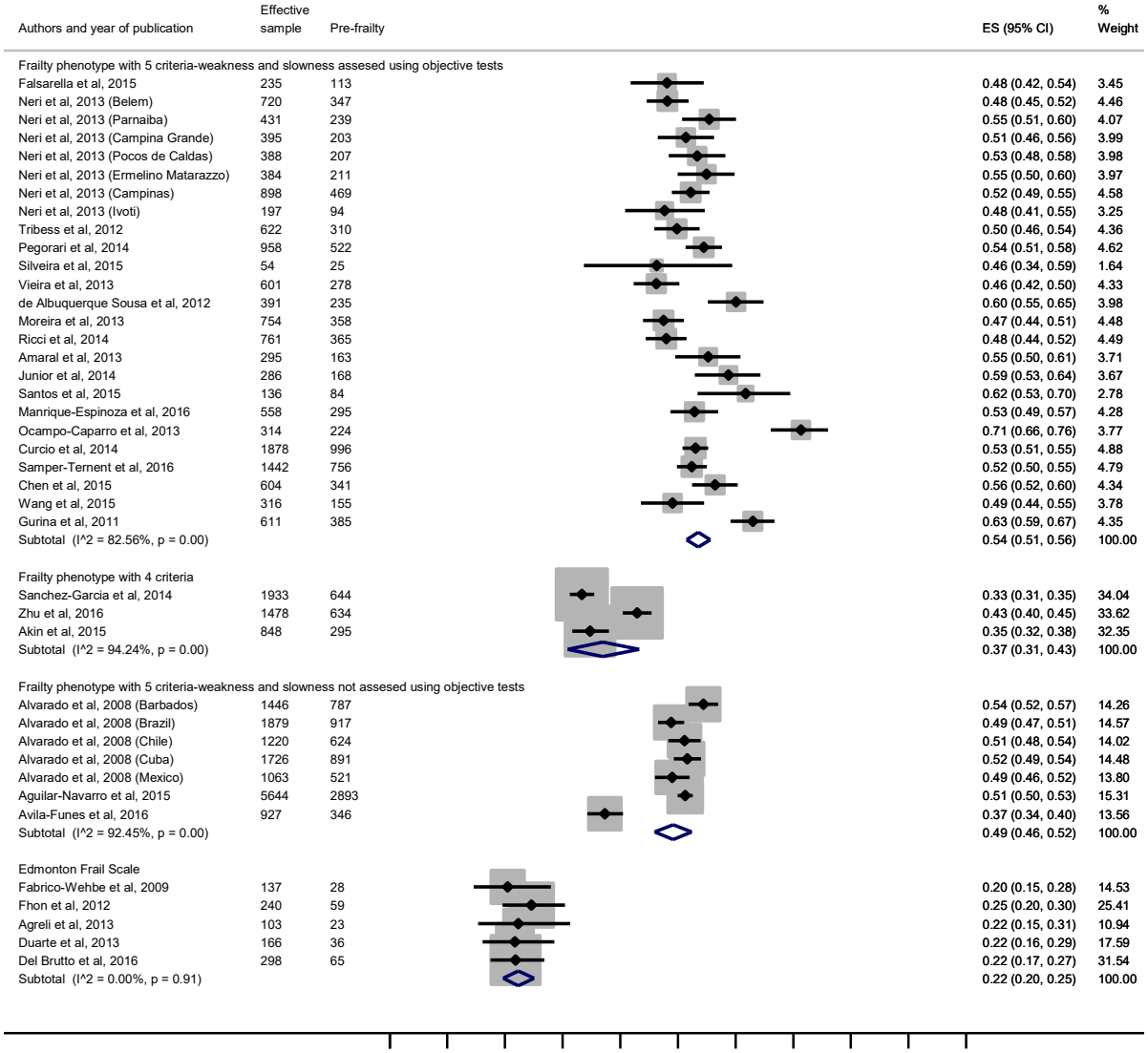
Fried Phenotype § = Fried Phenotype with 5 criteria-weakness and slowness assessed using self-reported questions (subjective)

*References for the tables in appendix B and C are listed below and are not same as the numbers in the text of this manuscript.

Appendix D- Random effects pooled prevalence of frailty stratified by frailty assessment method



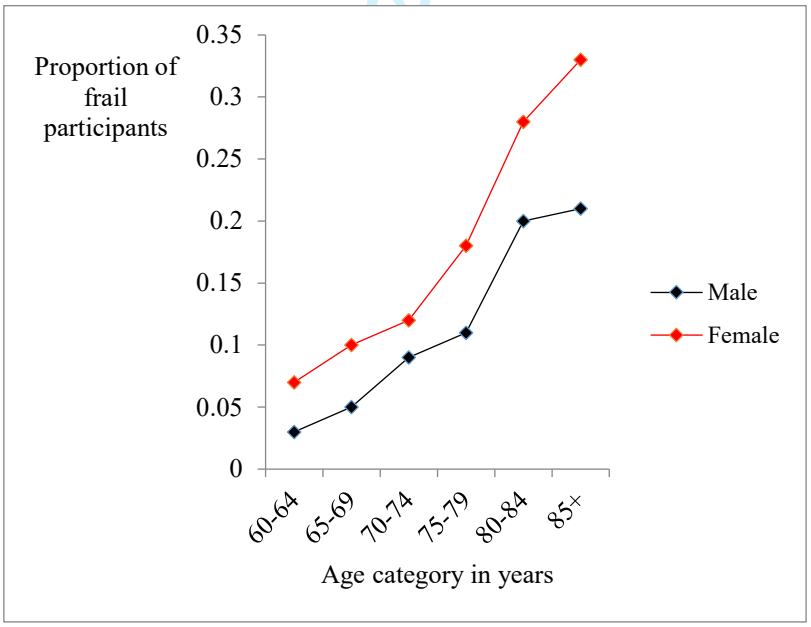
Appendix E- Random effects pooled prevalence of pre-frailty stratified by frailty assessment method



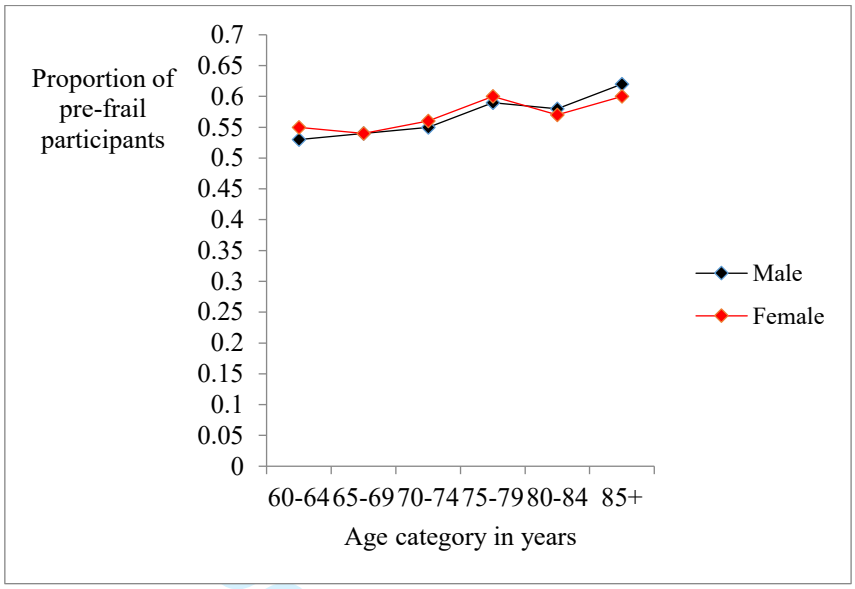
Appendix F- Pooled prevalence of frailty and pre-frailty by five years age categories for studies used Fried phenotype with 5 criteria where weakness and slowness assessed using objective tests

Age category	Number of studies	Number of participants	Pooled prevalence (%)	95% CI (%)	Cochran's Q	Degrees of freedom	I^2 (%)
Frailty							
60-64	7	1271	6	5-8	3.45	6	0.00
65-69	13	3176	8	6-11	64.4	12	81.4
70-74	13	3278	10	8-13	49.2	12	75.6
75-79	12	2106	15	12-18	37.9	11	71.0
80-84	12	940	23	18-29	30.5	11	64.0
85+	13	528	29	24-34	15.0	12	19.9
Pre-frailty							
60-64	7	1271	56	49-63	31.2	6	80.8
65-69	13	3176	53	48-57	60.7	12	80.2
70-74	13	3278	54	50-58	46.1	12	74.0
75-79	12	2106	58	55-61	17.6	11	37.5
80-84	12	940	56	53-60	8.4	11	0.00
85+	13	528	60	55-64	10.7	12	0.00

Appendix G- Pooled prevalence of frailty by age and sex for studies using all 5 Fried phenotype criteria with objective assessment for weakness and slowness



Appendix H- Pooled prevalence of pre-frailty by age and sex for studies using all 5 Fried phenotype criteria with objective assessment for weakness and slowness



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Prevalence of Frailty and Pre-Frailty among Community Dwelling Older Adults in Low and Middle Income Countries: A Systematic Review and Meta-Analysis

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Prevalence of Frailty and Pre-Frailty among Community Dwelling Older Adults in Low and Middle Income Countries: A Systematic Review and Meta-Analysis

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Abstract

Objective: To systematically review the research conducted on prevalence of frailty and pre-frailty among community dwelling older adults in low and middle income countries (LMICs) and to estimate the pooled prevalence of frailty and pre-frailty in community dwelling older adults in LMICs.

Design: Systematic review and meta-analysis. PROSPERO registration number is CRD42016036083.

Data sources: MEDLINE, EMBASE, AMED, Web of Science, CINAHL and WHO Global Health Library were searched from their inception to 12, September 2017.

Setting: Low and middle income countries.

Participants: Community dwelling older adults aged 60 years and above.

Results: We screened 7057 citations and 56 studies were included. Forty seven and 42 studies were included in the frailty and pre-frailty meta-analysis respectively. The majority of studies were from upper middle income countries. One study was available from low income countries. The prevalence of frailty varied from 3.9% (China) to 51.4% (Cuba) and prevalence of pre-frailty ranged from 13.4% (Tanzania) to 71.6% (Brazil). The pooled prevalence of frailty was 17.4% (95% CI=14.4-20.7%, I^2 =99.2) and pre-frailty was 49.3% (95% CI= 46.4-52.2%, I^2 =97.5). The wide variation in prevalence rates across studies was largely explained by differences in frailty assessment method and the geographic region. These findings are for the studies with minimum recruitment age 60, 65 and 70 years.

Conclusion: The prevalence of frailty and pre-frailty appears higher in community dwelling older adults in upper middle income countries compared to high income countries, which has

important implications for healthcare planning. There is limited evidence on frailty prevalence in lower middle and low income countries.

Key words: Ageing, Frailty syndrome, Epidemiology, Systematic review, Meta-analysis, LMICs

Strengths and limitations of this study

- This is the first systematic review and meta-analysis of the prevalence of frailty and pre-frailty among community dwelling older adults in low and middle income countries.
- We conducted a comprehensive literature search in six electronic databases with a comprehensive search strategy, including WHO Global Health Library to capture studies published regionally.
- No language restriction was imposed.
- Sub group analysis of prevalence of frailty and pre-frailty was performed with substantial number of studies, and meta-regression technique was used to identify the sources of heterogeneity between the studies.
- We did not include grey literature in this review.

INTRODUCTION

Population ageing is not confined to High Income Countries (HICs). People in Low and Middle Income Countries (LMICs) have increasing life expectancy with the advancement of health care services.[1] The pace of population ageing is faster in LMICs compared to HICs.[2] This creates an additional burden for these countries with growing economies as they have to tackle health, social and welfare issues associated with ageing populations.

Frailty is a health problem of older age with no universally agreed conceptual or operational definition. However, there is a common agreement that frailty is an important clinically identifiable state that increases the vulnerability to adverse outcomes due to the decline in reserve and functions in multiple physiological systems.[3] The Fried phenotype of frailty, comprised of five phenotypic criteria (unintentional weight loss, self-reported exhaustion, weakness, slowness and low physical activity)[4] and the frailty index, (comprised of a list of deficits),[5] are the most frequently used frailty assessment methods in the literature.[6] Longitudinal studies have identified several negative outcomes associated with frailty which can have a huge impact on individual lives and society as a whole. These include falls, worsening mobility, disability, hospitalization and increased risk of mortality. [4 5 7 8]

Pre-frailty is an intermediate state between frailty and non-frailty/robust that has higher risk of progressing to frailty.[9] Since frailty status is assessed using different assessment methods, most of the assessment methods have its own cut-off for pre-frailty status. For instance, having 1-2 criteria of five is considered as pre-frail for the Fried's phenotype.[4] Like frailty, pre-frailty is also associated with adverse health outcomes. Findings from a recent meta-analysis based on six prospective cohort studies suggested increased risk for faster onset of any type of cardio- vascular diseases in pre-frail versus robust.[10] Another longitudinal study also showed that pre-frail individuals are more likely to show persistent and new depressive

symptoms.[11] Evidence is emerging that frailty as a dynamic state with transitions between frailty statuses; frailty, pre-frailty and non-frailty[12-14] and there is potential for interventions to improve the health and wellbeing of both frail and pre-frail older adults.

A substantial amount of research on frailty has been conducted in HICs. According to a systematic review conducted in 2012, the weighted prevalence of frailty in HICs is 10.7% and pre-frailty is 41.6%.[15] There is some suggestion of a socio-economic gradient in frailty between HICs; one study from 15 European countries reported a lower mean frailty index in North and Western Europe compared to lower income countries in South and Eastern Europe.[16] In addition, the survival of frail older people was higher in countries with a higher relative income within Europe.[16] It is possible that the prevalence of frailty in LMICs is higher than HICs, given a steeper gradient in income. Alternatively the prevalence may be lower with a reduced life expectancy of older people in LMICs. A narrative review published in 2015 on frailty in developing countries found limited availability of studies and suggested that frailty occurs more frequently in developing countries.[17] However no studies are available up-to-date collating all the epidemiological findings available from LMICs to examine the burden of frailty in these countries. This is important to inform health care planning in these countries in the context of world-wide population ageing. The aim of this study was to conduct a systematic review and meta-analysis on prevalence of frailty and pre-frailty among community dwelling older adults in Low and Middle Income Countries.

METHODS

Search Strategy and selection criteria

We performed a comprehensive structured search in six electronic bibliographic databases. MEDLINE, EMBASE and AMED databases using OvidSP interface, Web of Science Core Collection, CINAHL Plus databases and WHO Global Health Library were searched from their inception to 12, September 2017. Two concepts; "frailty" and "low and middle income countries" were used to develop the electronic search strategy. The example Low and Middle Income Country filters developed by Cochrane organization in 2012 was used with slight modifications.[18] The World Bank country classification issued on 1, July 2017,[19] which is based on 2016 economic data was used to identify the countries that switched from low and middle income to high income countries in 2017 or vice versa. Studies in these countries were included only if the country belongs to low and middle income category during the time of data collection. The electronic search strategy was first developed for MEDLINE (appendix A, supplementary file) and then adapted accordingly to other databases. The electronic search strategy was developed with the support of specialist librarian (SP). Additionally reference lists of the selected articles were scanned and citation searches were performed in the Web of Science. The search was limited to full text articles as study quality assessment requires a detailed description on the methodology. No language restriction was imposed on the search.

The condition studied was frailty measured by any assessment method. The review was restricted to studies with community dwelling older adults aged 60 and above living in the LMICs. This age cut-off is in line with the United Nations's definition of older populations.[20] Studies with institutionalized or hospitalized adults, nursing home residents, outpatients of primary or secondary care clinics, or older adults belonging to specific disease groups were

excluded. Cross sectional studies conducted to assess the prevalence and associated factors of frailty, prospective follow-up studies that have baseline prevalence of frailty, cross sectional studies conducted to explore the association of frailty with some other health variable or disease (e.g. haemoglobin level, cardio vascular risk factors) were included in this review.

Identified citations were exported into EndNote X8 and duplicates were removed. In the first stage, the title and abstracts of the citations were screened against inclusion and exclusion criteria to identify potentially eligible citations. In the second stage, full-texts of potentially eligible articles were retrieved. Two reviewers (DDS and SH) independently reviewed the full-text articles to identify the articles meeting eligibility criteria. If multiple studies were available from the same cohort, the study with the largest sample and most information was included in the review. The agreement between the two raters was high with a kappa value of 0.84 (95% CI, 0.72 - 0.90). Disagreement between the reviewers was resolved through discussions and consulting senior researchers in the research team (KW, GR, and MCW).

Study quality assessment and data extraction

Selected articles were subjected to a quality assessment. Methodological rigor of the articles was assessed using eight criteria proposed by Loney et al[21] for the critical appraisal of prevalence literature. If a study achieved 3 criteria or less, it was excluded from the review. Study quality of all selected articles (61) was assessed by the first reviewer (DDS). The second reviewer (SH) assessed the study quality of a random 10 percent of articles to check for discrepancies.

Data extraction included information on study background (authors and year of publication, data source, study setting, study period), characteristics of the population (percentage of females in the study population, mean age, age range, number of frail and pre-frail participants in the total sample, and by sex and age), study methodology (study design,

effective sample, sampling technique, frailty assessment method) and study strengths and limitations. Authors were contacted requesting additional data required for sub group analysis.

Data analysis

The results of the systematic review are presented in tabular format and narratively synthesized. All statistical analyses were performed in Stata version 14 (StataCorp, College Station, Texas, USA). A random effects meta-analysis with 95% confidence intervals was performed to calculate the pooled prevalence of frailty and pre-frailty. A random effects model was chosen as there is a variation in the true effect from one study to another. And also, there was considerable heterogeneity of the study characteristics including geography, frailty assessment method, frailty cut-offs and recruitment age. When a study has used multiple assessment methods of frailty, the prevalence presented using Fried phenotype was used for the meta-analysis as it was the most commonly used assessment method in the literature.[22] The analysis was performed on Freeman-Tukey double arcsine transformed proportions to stabilize the variance. We used *metaprop random ftt* command.[23] Results were presented using forest plots. The main meta-analysis and sub group analysis excluded three studies, two studies with minimum recruitment age of 80 years or above and another study with minimum recruitment age 90 years or above as those based on much older populations with expected higher prevalence rates for frailty. The findings from these studies were reported separately.

Cochran's Q statistic was used to assess heterogeneity between the studies. $P<0.05$ was considered as evidence of heterogeneity. The I^2 statistic was further used to quantify the magnitude of the heterogeneity. I^2 values of 25%, 50% and 75% were considered as low, moderate and high heterogeneity respectively.[24] Funnel plots generated by *metafunnel*

command was used to visually inspect the existence of reporting biases and/or between study heterogeneity. In the absence of biases and/or between study heterogeneity, funnel plot will be symmetrical inverted funnel in shape.[25] However, this eye ball test is subjective. Hence, we used Egger's weighted regression test to measure the degree of funnel plot asymmetry. The null hypothesis for Egger's test is that symmetry exists in the funnel plot.[26 27] Stata *metabias* command was used.

Sub group analysis of frailty and pre-frailty prevalence was performed according to the frailty assessment method (Fried phenotype with 5 criteria where weakness and slowness assessed objectively using grip strength and gait speed, Fried phenotype with 5 criteria where weakness and slowness assessed using self-reported questions (subjective), Fried phenotype with 4 criteria, Edmonton Frail Scale (EFS), frailty index and, FRAIL scale). If the same cohort of participants had been assessed using different frailty assessment methods, we used that information in the subgroup analysis. However, studies that have used different frailty assessment methods to that mentioned above were excluded from the frailty and pre-frailty sub group analysis as they cannot be grouped in to a particular category i.e. Study of Osteoporotic Fractures index (SOF) and Cuban frailty criteria, Brief Frailty Instrument for Tanzania (B-FIT). Further sub group analyses by sex, age group (60-64, 65-69, 70-74, 75-79, 80-84, 85+), age and sex were performed with studies which had employed the Fried phenotype with 5 criteria where weakness and slowness assessed using objective tests. Two samples proportion test was used to compare the prevalence of frailty and pre-frailty by sex.

We performed a supplementary analysis to compare our findings with HICs. We used published data from a systematic review on prevalence of frailty which includes HICs only.[15] This review included 14 studies which had used Fried's phenotype of frailty assessment method. We estimated the random effects pooled prevalence of frailty and pre-frailty only

with the studies that have used the Fried phenotype with 5 criteria where weakness and slowness assessed using objective tests (10 studies). Minimum recruitment age of the participants included in this review was 65 years. For a fair comparison we calculated the random effects pooled prevalence of frailty and pre-frailty only with the studies of minimum recruitment age 65 years that have used same assessment method included in our review.

Random effects univariable and multivariable meta-regression were performed using *metareg* command to identify the potential sources of heterogeneity between the studies (demographic, geographical and methodological).[28] Three studies which used Study of Osteoporotic Fractures index (SOF), Cuban frailty criteria and Brief Frailty Instrument for Tanzania (B-FIT) were excluded from the analysis. The following explanatory variables were included in the models; mean age, percentage of females in the study sample, study quality assessment score, World Bank region classification (Latin America and the Caribbean, East Asia and Pacific, Europe and Central Asia, and South Asia), and frailty assessment method. All the variables were included in the multivariable model irrespective of their significance (p value) in univariable analysis. Variables with $p<0.05$ were considered as significant. The systematic review protocol of this study registered in PROSPERO and number is (CRD42016036083). This systematic review and meta-analysis have been reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2009 checklist is attached separately).[29]

RESULTS

Study characteristics

The search yielded 10253 records, with 7057 records left after removing duplicates. Fifty six studies meeting all eligibility criteria were included in the systematic review (figure 1). Forty seven and 42 studies were included in the meta-analysis of frailty and pre-frailty respectively.

Figure 1: Study selection

The study quality assessment score of the studies included ranged from 3.5 to 7.5, with a mean score of (standard deviation) 6.0 (1.07). Quality assessment results of the studies are presented in appendix B (supplementary file). The characteristics of included studies are described in appendix C (supplementary file). Fifty studies have been published between 2012 and 2017. The majority of the studies were from the Latin America and the Caribbean region, predominantly from Brazil (n=24). Most of the studies had utilized data from large population based cross sectional or longitudinal studies on ageing.

The sample size of the studies varied (range 54 to 12373) and the minimum recruitment age of the study participants varied from 60 to 90 years. The minimum age at recruitment of the study participants was 60 years in 30 studies, 65 years in 19 studies, 70 years in 4 studies, 80 years in 2 studies and 90 years in one study. Fifty two studies had reported the percentage of females in the study samples and it varied from 48.1% to 100.0%, with more than half of participants female in all except three studies. Forty two studies reported the mean age (42/56) of the participants, which ranged from 68.2 to 77.2 years after excluding three studies with minimum recruitment age 80 years and above (2 studies) and 90 years and above (1 study).

Studies used various frailty assessment methods. The Fried phenotype was the most extensively used method. Researchers had operationalized the Fried phenotype differently. We identified three broad categories based on the number of phenotypic criteria used and measures used to operationalize those criteria. Those are Fried phenotype with 5 criteria-weakness and slowness assessed using objective tests, Fried phenotype with 5 criteria-weakness and slowness assessed using self-reported questions (subjective) and Fried phenotype with only 4 criteria.

Prevalence of frailty and pre-frailty

Irrespective of the frailty assessment method, the prevalence of frailty varied from 3.9% in China (Fried phenotype with 5 criteria- weakness and slowness assessed using objective tests) to 51.4% in Cuba (Cuban frailty criteria) and prevalence of pre-frailty ranged from 13.4% in Tanzania (Brief Frailty Instrument for Tanzania, B-FIT) to 71.6% in Brazil (Fried Phenotype with 5 criteria- weakness and slowness measured objectively) for the studies with minimum recruitment age 60 years, 65 years and 70 years. There was one study in those aged 90 years+, reporting 61.8% participants as frail using frailty index (not reported pre-frailty). Another study with aged 80 years+ had not reported a cut-off value for frailty index to define frail participants. Instead, authors had reported six levels based on the value of frailty index and the percentage of participants belongs to each level. The other study with aged 80 years+ reported 14.8% and 63.8% participants as frail and pre-frail respectively using Fried phenotype with 5 criteria- weakness and slowness assessed using objective tests. When restricting to the studies that used Fried phenotype with five criteria and assessed the weakness and slowness objectively, the prevalence of frailty varied from 3.9% (China) to 26.0% in India. The prevalence of pre-frailty varied from 40.7% to 71.6% in Brazil.

Pooled prevalence of frailty and pre-frailty

Descriptions of included studies in the meta-analysis are presented in table 1. Sixty nine prevalence estimates (47 studies), corresponding to a total of 75,133 community dwelling older adults, were included in the frailty meta-analysis. The random-effects pooled prevalence of frailty in community dwelling older adults was 17.4% (95% CI=14.4-20.7%). Cochran's Q and I^2 indicated a substantial heterogeneity between included studies (Q=8756.8, df=68, p<0.001; I^2 =99.2%) (figure 2). Funnel plot asymmetry (figure 3) revealed

evidence of reporting biases and/or between study heterogeneity. Results of Egger's weighted regression test further confirmed the funnel plot asymmetry (p=0.042).

Table 1: Descriptions of the studies included in the meta-analysis of prevalence of frailty and pre-frailty

Authors and year of publication	Country	World Bank region classification	World Bank income classification	Age (years)	Frailty assessment method	Effective sample	Prevalence (%)	
							Frailty	Pre-frailty
Tribess et al, 2012[30]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 60	Fried Phenotype ǂ	622	19.9	49.8
Júnior et al, 2014[31]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 60	Fried Phenotype ǂ	286	23.8	58.7
Pegorari et al, 2014[32]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 60	Fried Phenotype ǂ	958	12.8	54.5
Santos et al, 2015[33]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 60	Fried Phenotype ǂ	136	16.9	61.8
Closs et al, 2016[34]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 60	Fried Phenotype ǂ	521	21.5	51.1
Mello et al, 2017[35]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 60	Fried Phenotype ǂ	137	12.4	61.3
de Albuquerque Sousa et al, 2012[36]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	391	17.1	60.1
dos Santos Amaral et al, 2013[37]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	295	18.6	55.3
Moreira et al, 2013[38]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	754	9.5	47.5
Neri et al, 2013[39] (Belem)	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	720	10.8	48.2
Neri et al, 2013[39] (Parnaiba)	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	431	9.7	55.5
Neri et al, 2013[39] (Campina Grande)	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	395	8.9	51.4
Neri et al, 2013[39] (Pocos de Caldas)	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	388	9.3	53.4
Neri et al, 2013[39] (Ermelino Matarazzo)	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	384	8.1	54.9
Neri et al, 2013[39] (Campinas)	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	898	7.7	52.2
Neri et al, 2013[39] (Ivoti)	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	197	8.6	47.7
Vieira et al, 2013[40]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	601	8.7	46.3
Ricci et al, 2014[41]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	761	9.7	48.0
Silveira et al, 2015[42]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	54	11.1	46.2
Calado et al, 2016[43]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	385	9.1	49.6
Augusti et al, 2017[44]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	306	21.5	71.6
Ferriolli et al, 2017[45] (Recife)	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	556	12.1	66.9
Ferriolli et al, 2017[45] (Juiz de Fora)	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	412	15.5	63.1
Ferriolli et al, 2017[45] (Fortaleza)	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype ǂ	481	10.4	63.6
Ocampo-Chaparro et al, 2013[46]	Colombia	Latin America & the Caribbean	Upper middle income	≥ 60	Fried Phenotype ǂ	314	12.7	71.3
Curcio et al, 2014[47]	Colombia	Latin America & the Caribbean	Upper middle income	≥ 60	Fried Phenotype ǂ	1878	12.2	53.0
Samper-Ternent et al, 2016[48]	Colombia	Latin America & the Caribbean	Upper middle income	≥ 60	Fried Phenotype ǂ	1442	9.4	52.4
Sánchez-García et al, 2017[49]	Mexico	Latin America & the Caribbean	Upper middle income	≥ 60	Fried Phenotype ǂ	1252	11.2	50.3
Moreno-Tamayo et al, 2017[50]	Mexico	Latin America & the Caribbean	Upper middle income	≥ 70	Fried Phenotype ǂ	657	11.9	51.9
Chen et al, 2015[51]	China	East Asia and Pacific	Upper middle income	≥ 60	Fried Phenotype ǂ	604	12.7	56.5
Wu et al, 2017[52]	China	East Asia and Pacific	Upper middle income	≥ 60	Fried Phenotype ǂ	5290	6.3	51.3
Dong et al, 2017[53]	China	East Asia and Pacific	Upper middle income	≥ 60	Fried Phenotype ǂ	1188	3.9	45.9
Wang et al, 2015[54]	China	East Asia and Pacific	Upper middle income	≥ 65	Fried Phenotype ǂ	316	14.2	49.1
Badrasawi et al, 2017[55]	Malaysia	East Asia and Pacific	Upper middle income	≥ 60	Fried Phenotype ǂ	473	8.9	61.7
Kashikar et al, 2016[56]	India	South Asia	Lower middle income	≥ 65	Fried Phenotype ǂ	250	26.0	63.6
Gurina et al, 2011[57]	Russia	Europe and Central Asia	Upper middle income	≥ 65	Fried Phenotype ǂ	611	21.1	63.0
Alvarado et al, 2008[58] (SABE wave 1)	Barbados	Latin America & the Caribbean	Upper middle income	≥60	Fried phenotype§	1446	26.7	54.4
Alvarado et al, 2008[58] (SABE wave 1)	Brazil	Latin America & the Caribbean	Upper middle income	≥60	Fried phenotype§	1879	40.6	48.8
Alvarado et al, 2008[58] (SABE wave 1)	Chile	Latin America & the Caribbean	Upper middle income	≥60	Fried phenotype§	1220	42.6	51.4
Alvarado et al, 2008[58] (SABE wave 1)	Cuba	Latin America & the Caribbean	Upper middle income	≥60	Fried phenotype§	1726	39.0	51.6
Alvarado et al, 2008[58] (SABE wave 1)	Mexico	Latin America & the Caribbean	Upper middle income	≥60	Fried phenotype§	1063	39.5	49.0

Authors and year of publication	Country	World Bank region classification	World Bank income classification	Age (years)	Frailty assessment method	Effective sample	Prevalence (%)	
							Frailty	Pre-frailty
Aguilar-Navarro et al, 2015[59] (MHAS wave 1)	Mexico	Latin America & the Caribbean	Upper middle income	≥60	Fried phenotype§	5644	37.2	51.3
Avila-Funes et al, 2016[60]	Mexico	Latin America & the Caribbean	Upper middle income	≥70	Fried phenotype§	927	14.1	37.3
Sanchez-Garcia et al, 2014[61]	Mexico	Latin America & the Caribbean	Upper middle income	≥60	Fried Phenotype*	1933	15.7	33.3
Akin et al, 2015[62] (KEHES)	Turkey	Europe and Central Asia	Upper middle income	≥60	Fried Phenotype*	848	27.8	34.8
Zhu et al, 2016[63]	China	East Asia and Pacific	Upper middle income	≥ 70	Fried Phenotype*	1478	12.0	42.9
Jotheeswaran et al, 2015[64]	China (Urban)	East Asia and Pacific	Upper middle income	≥ 65	Fried Phenotype*	989	7.8	-
Jotheeswaran et al, 2015[64]	China (Rural)	East Asia and Pacific	Upper middle income	≥ 65	Fried Phenotype*	1002	8.7	-
Jotheeswaran et al, 2015[64]	Cuba (Urban)	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype*	2637	21.0	-
Jotheeswaran et al, 2015[64]	Dominican Republic (Urban)	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype*	1706	34.6	-
Jotheeswaran et al, 2015[64]	India (Urban)	South Asia	Lower middle income	≥ 65	Fried Phenotype*	748	11.4	-
Jotheeswaran et al, 2015[64]	Mexico (Urban)	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype*	909	10.1	-
Jotheeswaran et al, 2015[64]	Mexico (Rural)	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype*	933	8.5	-
Jotheeswaran et al, 2015[64]	Peru (Urban)	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype*	1245	25.9	-
Jotheeswaran et al, 2015[64]	Peru (Rural)	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype*	507	17.2	-
Jotheeswaran et al, 2015[64]	Venezuela (Urban)	Latin America & the Caribbean	Upper middle income	≥ 65	Fried Phenotype*	1697	11.0	-
Fhon et al, 2012[65]	Brazil	Latin America & the Caribbean	Upper middle income	≥60	EFS	240	39.2	24.6
Agreli et al, 2013[66]	Brazil	Latin America & the Caribbean	Upper middle income	≥60	EFS	103	30.1	22.3
Duarte et al, 2013[67]	Brazil	Latin America & the Caribbean	Upper middle income	≥60	EFS	166	39.2	21.7
Del Brutto et al, 2016[68]	Ecuador	Latin America & the Caribbean	Upper middle income	≥60	EFS	298	31.2	22.0
Fabricio-Wehbe et al, 2009[69]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	EFS	137	31.4	20.4
Carneiro et al, 2016[70]	Brazil	Latin America & the Caribbean	Upper middle income	≥ 65	EFS	511	41.3	-
Woo et al, 2015[71]	China	East Asia and Pacific	Upper middle income	≥ 65	Frailty Index	6320 (urban)	17.0	-
						978 (rural)	5.2	-
Sathasivam et al, 2015[72]	Malaysia	East Asia and Pacific	Upper middle income	≥ 60	Frailty Index	789	5.7	67.7
Perez-Zepeda et al, 2016[73]	Mexico	Latin America & the Caribbean	Upper middle income	≥ 60	Frailty index	7108	45.2	-
Galban et al, 2009[74]	Cuba	Latin America & the Caribbean	Upper middle income	≥ 60	Cuban frailty criteria	541	51.4	-
Boulos et al, 2016[75]	Lebanon	Middle East and North Africa	Upper middle income	≥ 65	SOF frailty index	1120	36.4	30.4
Gray et al, 2017[76]	Tanzania	Sub-Saharan Africa	Low income	≥70	B-FIT	941	4.6	13.4

Fried Phenotype ǂ - Fried Phenotype with 5 criteria-weakness and slowness assessed using objective tests
Fried Phenotype §- Fried Phenotype with 5 criteria-weakness and slowness assessed using self-reported questions (subjective)
Fried Phenotype*- Fried phenotype with 4 criteria
EFS-Edmonton Frail Scale
SOF- Study of Osteoporotic Fractures (SOF) frailty index
B-FIT- Brief Frailty Instrument for Tanzania

Figure 2: Random effects pooled prevalence of frailty among community dwelling older adults in low and middle income countries

Figure 3: Funnel plot for assessing publication or other types of biases in meta-analysis of prevalence of frailty

Fifty four prevalence estimates (42 studies) corresponding to 47,302 participants were included in the pre-frailty meta-analysis. The random-effects pooled prevalence of pre-frailty in community dwelling older adults was 49.3% (95% CI= 46.4-52.2%). High heterogeneity was observed between included studies (Q=2082.6, df=53, p<0.001; I^2 =97.5%) (figure 4). Asymmetric funnel plot (figure 5) suggested the existence of reporting biases and/or between study heterogeneity. However, results of Egger's weighted regression test was insignificant indicating no funnel plot asymmetry (p=0.817).

Figure 4: Random effects pooled prevalence of pre-frailty among community dwelling older adults in low and middle income countries

Figure 5: Funnel plot for assessing publication or other types of biases in meta-analysis of prevalence of pre-frailty

Subgroup analyses

The pooled prevalence varied by the assessment method and the highest prevalence of frailty was reported for the EFS, 35.9% (95% CI= 31.7-40.2%, I^2 =61.9, p=0.022). The lowest prevalence of frailty was reported for FRAIL scale, 12.4% (95% CI= 8.4-17.1%). The pooled prevalence of frailty for the Fried phenotype with 5 criteria- weakness and slowness assessed using objective tests was 12.7% (95% CI= 10.9-14.5%, I^2 =94.8, p<0.001) (appendix D, supplementary file). Results for pooled prevalence of pre-frailty stratified by frailty assessment method is presented in appendix D (supplementary file).

Twenty four prevalence estimates were available from 24 studies using the same assessment method (Fried Phenotype with objective tests) for sex stratified analysis of prevalence of frailty and pre-frailty. In total there were 10,507 and 15,458 male and female participants respectively. The pooled prevalence of frailty in males was 11.1% (95% CI= 8.9-13.4%, I^2 =91.4, p<0.001) compared to 15.2% (95% CI= 12.5-18.1%, I^2 =95.2, p<0.001) in females. Frailty prevalence was significantly higher in females compared to males (Z=-7.38, p<0.001). The pooled prevalence of pre-frailty in males was 53.8% (95% CI=51.3-56.3%, I^2 =80.9, p<0.001) and females was 56.3% (95% CI= 54.0-58.7%, I^2 =86.2, p<0.001). Similar to frailty, there was a statistically significant sex difference in pre-frailty (Z=-3.51, p<0.001).

The prevalence of frailty increased gradually with advancing age (appendix E, supplementary file). The prevalence considerably increased after age 75 years. The prevalence of pre-frailty also slightly increased with advancing age and was above 50% in all age groups. An age related incremental rise in frailty was evident even after stratification by sex (appendix F, supplementary file). Prevalence of frailty was higher in females in all five year age bands. There was no age related trend for pre-frailty after stratification by sex (appendix G, supplementary file).

Supplementary analysis

Ten prevalence estimates (10 studies), corresponding to a total of 27,660 community dwelling older adults from HICs and twenty one prevalence estimates (13 studies), corresponding to a total of 9,586 community dwelling older adults from middle income countries, were included in the frailty meta-analysis. The random-effects pooled prevalence of frailty in community dwelling older adults in HICs and middle income countries were 8.2% (95% CI=5.7-11.2%) (appendix H, supplementary file) and 12.3% (95% CI 10.4-14.4%) (appendix I, supplementary file) respectively. The prevalence of frailty in older adults

from middle income countries was significantly higher compared to the older adults residing in HICs, (Z=-8.86, p<0.001). However, it is also of note that studies included in the meta-analysis of HICs were predominantly from United States whereas studies included in the middle income countries meta-analysis were predominantly from Brazil and all the countries belong to upper middle income category except one study from India. The pooled prevalence of frailty except the study from India was 11.8% (95% CI=10.0-13.6%) and still significantly higher compared to HICs.

The random effects pooled prevalence of pre-frailty in community dwelling older adults in HICs and middle income countries were correspondingly 43.9% (95% CI 40.9-46.9%) (appendix J, supplementary file) and 55.3% (95% CI 52.0-58.6%) (appendix K, supplementary file). Like frailty, prevalence of pre-frailty also significantly higher among the older adults in middle income countries compared to the higher income countries (Z=-17.14, p<0.001).

Meta-regression

After adjusting for all the other study characteristics in a multivariable meta-regression model, there remained statistically significant differences in frailty prevalence between different assessment methods. Use of EFS, frailty index and Fried phenotype (5 criteria, weakness and slowness assessed using self-reported questions (subjective)) were associated with a frailty prevalence approximately 20% higher than the reference method (Fried phenotype 5 criteria with objective tests). Geographic region was also a statistically significant predictor of frailty. The variables included in the multivariable model (mean age, % of females in the sample, study quality assessment score, geographic region and frailty assessment method) explained 58.4% of variability between the studies included in the analysis (table 2).

Table 2: Univariable and multivariable meta-regression results

Characteristic	Univariable analysis				Multivariable analysis			
	No of estimates	β (95% CI)	p value	Adjusted R^2 (%)	No of estimates	β (95% CI)	p value	Adjusted R^2 (%)
Mean age, years (per unit increase)	41	0.003 (-0.012, 0.018)	0.665	-2.48	41	0.003 (-0.009, 0.017)	0.570	58.41
Percentage of females in the sample (per unit increase)	53	0.002 (-0.001, 0.007)	0.190	0.96	41	-0.000 (-0.004, 0.004)	0.962	
Study quality assessment score (per unit increase)	53	-0.007 (-0.046, 0.031)	0.697	-1.77	41	0.015 (-0.020, 0.051)	0.379	
World Bank region classification *(Reference: Latin America and the Caribbean)*	38			19.96	29			
East Asia and Pacific	11	-0.138 (-0.212,-0.063)	0.001		8	-0.105 (-0.177,- 0.033)	0.005	
Europe and Central Asia	2	0.014 (-0.144, 0.173)	0.856		2	0.068 (-0.051, 0.189)	0.252	
South Asia	2	-0.051 (-0.217-0.114)	0.535		2	0.001 (-0.129, 0.132)	0.982	
Frailty assessment method *(Reference: Frailty phenotype with 5 criteria, weakness and slowness assessed using objective tests)*	23			47.11	20			
Edmonton Frail Scale	6	0.222 (0.124, 0.319)	0.000		6	0.215 (0.120, 0.309)	0.000	
Frailty index	4	0.053 (-0.041, 0.149)	0.264		2	0.171 (0.056, 0.286)	0.005	
Fried phenotype with 4 criteria	13	0.026 (-0.037, 0.089)	0.410		12	0.032 (-0.035, 0.100)	0.342	
Fried phenotype with 5 criteria, weakness and slowness assessed using self-reported questions (subjective)	7	0.206 (0.129, 0.283)	0.000		1	0.223 (0.065, 0.382)	0.007	

DISCUSSION

Summary of main findings

Only one epidemiological study on frailty was found from countries with low income economies[76] (US$ 1,005 or less) according to World Bank Classification, 2017.[19] Of countries with lower-middle-income economies (US$ 1,006 to US$ 3,955) we only found two studies both from India. One was a study site of a multi-country study[64] and the other one was a small community based cross sectional study.[56] All the other studies have been conducted in countries with upper-middle-income economies (US$ 3,956 to US$ 12,235) indicating income inequality in frailty research.

The random effects pooled prevalence of frailty and pre-frailty in community dwelling older adults were 17.4% (95% CI=14.4-20.7%) and 49.3% (95% CI= 46.4-52.2%) respectively. Frailty was significantly higher in females compared to males and as expected increased with age. This finding is consistent with previous research.[15 58 77-79] Interestingly, the prevalence of pre-frailty was also slightly increasing across all age groups at around half the participants. Both the prevalence of frailty and pre-frailty appeared significantly higher in community dwelling older adults in upper middle income countries compared to high income countries.

Comparison with existing literature

The prevalence of frailty and pre-frailty in low and middle income countries in this review appeared to be higher than the pooled prevalence in HICs reported previously (10.7%, (95% CI= 10.5-10.9%)) and 41.6% (95% CI= 41.2-42.0%) respectively.[15] However, it is also of note that the participants in HICs included people aged 65 years and above whereas 50% of studies in our meta-analysis included participants 60 years and above. Given that prevalence of frailty increases with age, when participants of a higher age group are selected, a higher prevalence would be expected. Our meta-analysis included 18 studies (36 estimates) with a

population aged 65 years and above. The prevalence of frailty of this sub sample was 14.6% (95% CI= 11.9-17.4%) and still higher compared to HICs. In the review of frailty in HICs, most studies were from Europe and North America. Studies included in our review were predominantly from Latin America and belong to the countries with upper middle income economies, with little representation of lower middle and low income countries. A recent meta-analysis in Latin America and Caribbean showed consistent findings to our study, with nearly one out of five older adult defined as frail.[80]

We found lower prevalence rates when we restricted the meta-analysis only to the Fried phenotype with five criteria, including objective measures of weakness and slowness. This found a pooled prevalence of frailty of 12.7% and pre-frailty of 55.2%. The review on frailty and pre-frailty which included only HICs has simply reported the weighted prevalence of frailty and pre-frailty.[15] Given the heterogeneity of the studies along with the actual differences of frailty estimates in different populations, we performed a supplementary analysis for a fair comparison of frailty estimates between HICs and middle income countries (no studies were available from low income countries using the same frailty assessment method). Results indicated significantly higher prevalence of frailty and pre-frailty among community dwelling older adults in middle income countries compared to the HICs. Another review of the prevalence of frailty measured by the Fried phenotype based on community dwelling older adults above 65 years in nationally representative samples reported lower prevalence to our estimate except in the countries of Southern Europe (France, Italy, Greece, and Spain).[81] Lower prevalence of frailty is also observed in high income Asian countries (Japan, Singapore and Taiwan).[79 82-84]

In contrast to these findings, a single multi-country study conducted with data from 14 high income countries in Europe and 6 low and middle income countries (China, Ghana, India, Mexico, Russian Federation and South Africa) reported higher frailty level (high mean frailty

index) in high income countries compared to the low income countries.[77] This study included nationally representative samples of adults aged 50 years and older. They also found an inverse association between level of frailty and income and education in both high and low income countries. Individuals with poor education and low income were more likely to be frail. Higher levels of frailty in high income countries could be due to the higher survival rate of participants with advanced health care and social protection. On the other hand, as the frailty index is based on a list of deficits including diagnosed diseases, many medical conditions could be under reported/diagnosed in the participants in low and middle income countries. Similarly, in most low and middle income countries where access to continued care is lacking, maintenance of medical records are poor making it difficult to use cumulative deficit models.

In our study, even among the studies using Fried phenotype with objective criteria, there was considerable variation in operationalizing the five phenotypic criteria. Furthermore, the approach to deriving frail cut-offs for weakness, slowness and physical activity criteria were varied. Of thirty studies 17 have calculated their population specific cut-offs based on the anthropometry of their own study populations. Eight studies have used the cut-offs developed by Fried et al in the Cardiovascular Health Study (CHS).[4] The pooled prevalence of frailty is higher with the studies used CHS cut-offs compared to the studies used own population specific cut-offs. However, the pooled prevalence of pre-frailty was similar in both groups. Similarly the number of deficits used in frailty index and cut off points for defining frailty and pre-frailty status were inconsistent.[71-73] A further meta-analysis with all available studies including both higher and the lower and middle income countries would be valuable, controlling for frailty assessment method, sex and age composition of the sample. In addition methodologically comparable studies across countries are required to study the true population difference of frailty.

Strength and weaknesses

This is the first systematic review and meta-analysis on prevalence of frailty and pre-frailty among community dwelling older adults in LMICs. The strengths of our study include; we conducted a comprehensive literature search in six electronic databases with a comprehensive search strategy, including WHO Global Health library to capture studies published regionally. No language restriction, sub group analysis of prevalence of frailty and pre-frailty with substantial number of studies, and using a meta-regression technique to identify the sources of heterogeneity between the studies, contacting authors to get the additional information of the studies required for sub group analyses were also strengths.

Both funnel plot asymmetry and the results of the Egger's weighted regression test indicated the presence of reporting biases and/or between study heterogeneity in the random effects meta-analysis of frailty. The nature of our study effect (prevalence) is unlikely to be affected by publication bias. However, publication bias could also be affected by study size, funding source or research group.[27] We noted that majority of the studies included in our meta-analysis have large samples. Multiple sources have been identified that could affect funnel plot asymmetry including reporting biases (publication bias, selective outcome reporting, selective analysis reporting), poor methodological quality, true heterogeneity, artefactual and chance.[25 26] In our case we believe that the funnel plot asymmetry is mainly due to the true heterogeneity between the studies mainly because of the use of different frailty assessment methods. And also, it is possible to have a true underlying difference of frailty prevalence in different populations. Another limitation of this study was non-inclusion of grey literature.

Implications for practice

The findings of the study suggest that the prevalence of frailty appears higher among community dwelling older adults in upper middle income countries compared to high income

countries. One study was identified from low income countries and two studies from a lower middle income country. Despite evidence that populations are rapidly ageing in many of these countries, we do not currently know the prevalence of frailty in these populations to inform health and social care planning. Research is required from low and lower middle income countries with rapidly ageing populations to estimate burden of frailty and to understand how frailty affects the day-to-day lives of older people. Furthermore, a consensus is required on methods of assessing frailty to allow for more robust comparisons across populations.

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Competing interests

The authors declare that they have no competing interests.

Ethical Clearence

This study is a systematic review and meta-analysis using already published litearature. Hence, ethical approval is not required.

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Contributors

Dhammika Deepani Siriwardhana (DDS), Kate Walters (KW) and Greta Rait (GR) conceived the idea of this systematic review. DDS designed, conducted the study and drafted the manuscript. Sarah Hardoon (SH) was the secondary reviewer of the systematic review and involved with screening, data extraction, study quality assessment, data analysis and provided important intellectual facts to revise the manuscript. KW, GR and Manuj Chrishantha Weerasinghe (MCW) provided important feedback at various stages of the study; devising the protocol, resolving the disagreements between DDS and SH at the study selection

process, clarifying the issues related to study quality assessment and interpreting the findings and providing important intellectual facts to revise the manuscript.

Data sharing statement

No additional data available.

Figure 1: Study selection

Figure 2: Random effects pooled prevalence of frailty among community dwelling older adults in low and middle income countries

Figure 3: Funnel plot for assessing publication or other types of biases in meta-analysis of prevalence of frailty

Figure 4: Random effects pooled prevalence of pre-frailty among community dwelling older adults in low and middle income countries

Figure 5: Funnel plot for assessing publication or other types of biases in meta-analysis of prevalence of pre-frailty

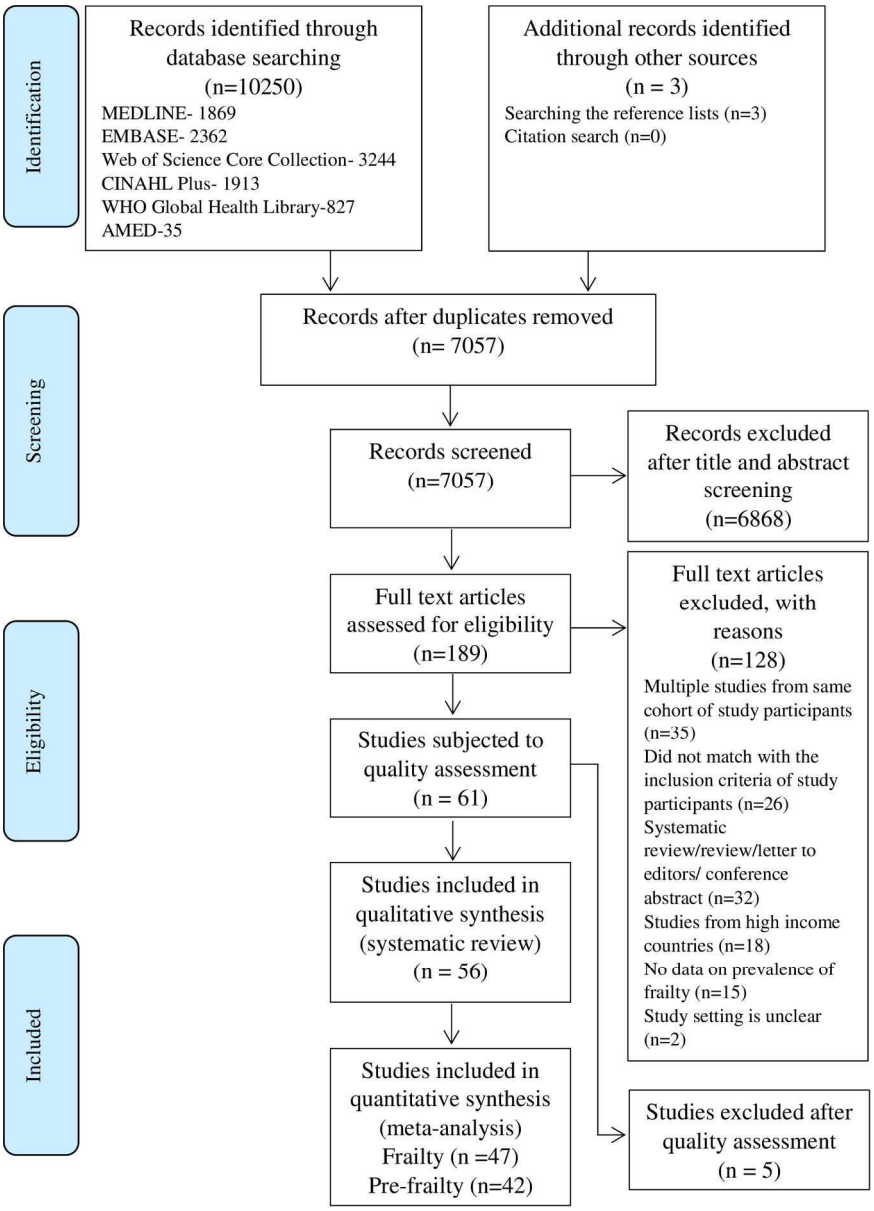


Figure 1: Study selection

145x200mm (300 x 300 DPI)

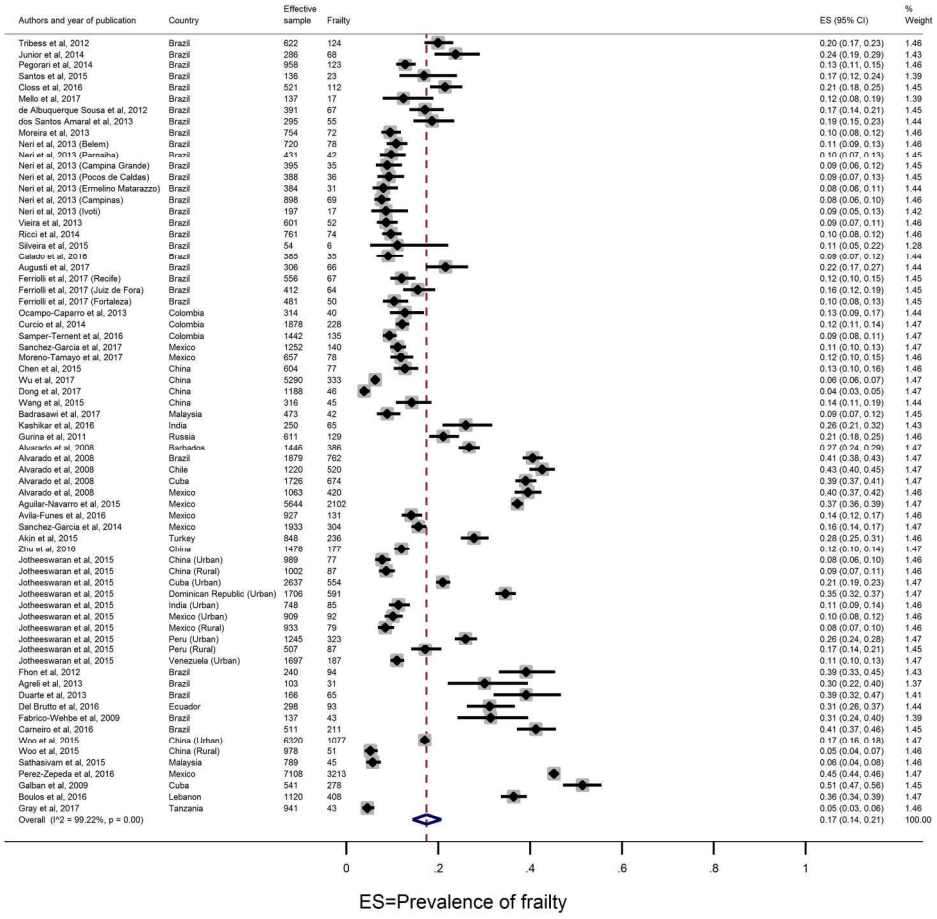


Figure 2: Random effects pooled prevalence of frailty among community dwelling older adults in low and middle income countries

190x185mm (300 x 300 DPI)

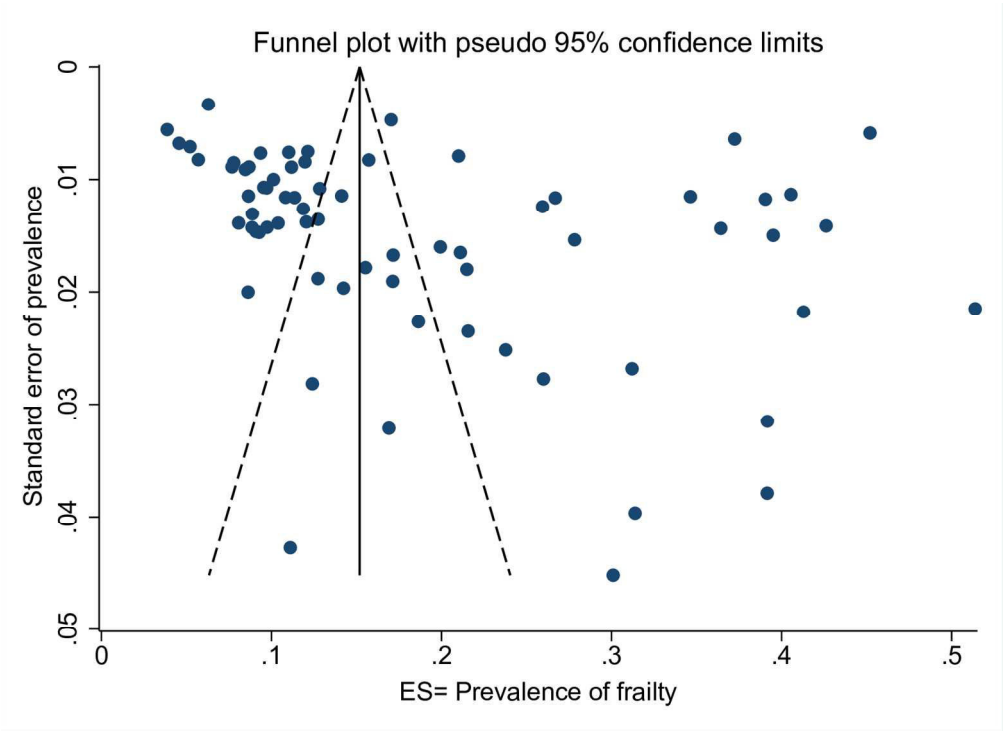


Figure 3: Funnel plot for assessing publication or other types of biases in meta-analysis of prevalence of frailty

139x101mm (300 x 300 DPI)

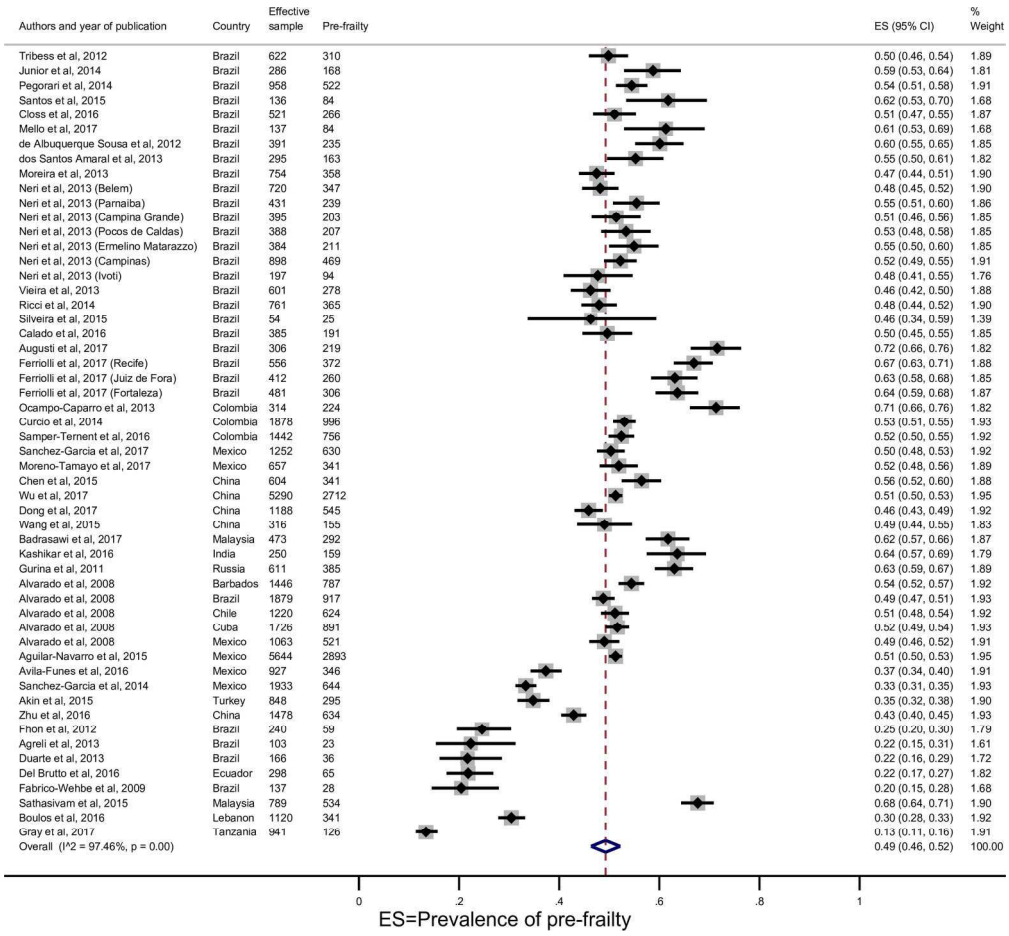


Figure 4: Random effects pooled prevalence of pre-frailty among community dwelling older adults in low and middle income countries

190x175mm (300 x 300 DPI)

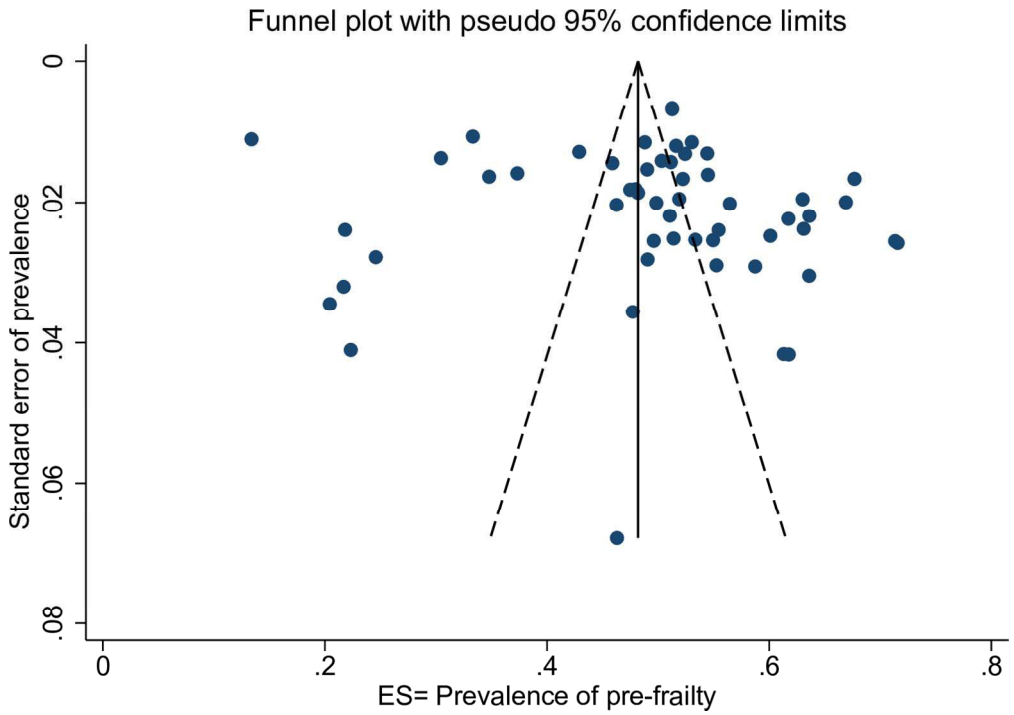


Figure 5: Funnel plot for assessing publication or other types of biases in meta-analysis of prevalence of pre-frailty

132x93mm (300 x 300 DPI)

Appendix A- MEDLINE Search Strategy

1. Frail Elderly.sh,kf.

2. (frail* or geriatric syndrome* or geriatric disorder*).ti,ab.

3. ((elder* or old* or senior* or geriatric*) adj4 function* adj4 (declin* or impair*)).af.

4. 1 or 2 or 3

5. Developing Countries.sh,kf.

6. (Africa* or Asia* or Caribbean* or West Indi* or South America* or Latin America* or Central America*).hw,kf,ti,ab,cp.

7. ((developing or less* developed or under developed or underdeveloped or middle income or low* income or underserved or under served or deprived or poor*) adj (countr* or nation? or population? or world)).ti,ab.

8. ((developing or less* developed or under developed or underdeveloped or middle income or low* income) adj (economy or economies)).ti,ab.

9. (low* adj (gdp or gnp or gni or gross domestic or gross national)).ti,ab.

10. (low adj3 middle adj3 countr*).ti,ab.

11. (lmic or lmics or third world or lami countr*).ti,ab.

12. transitional countr*.ti,ab.

13. (Afghanistan or Albania* or Algeria* or Angola* or Antigua or Barbuda or Argentin* or Armenia* or Aruba or Azerbaijan or Bahrain or Bangladesh* or Barbados or Benin or Byelarus or Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or Herzegovina or Hercegovina or Botswana or Brasil* or Brazil* or Bulgaria* or Burkina Faso or Burkina Fasso or Upper Volta or Burundi or Urundi or Cambodia* or Khmer Republic or Kampuchea or Cameroon or Cameroons or Cameron or Camerons or Cape Verde or Cabo Verde or Central African Republic or Chad or Chile or China or Chinese or Colombia* or Comoros or Comoro Islands or Comores or Mayotte or Congo or Zaire or Costa Rica or Cote d'Ivoire or Ivory Coast or Croatia or Cuba* or Cyprus or Czechoslovakia or Czech Republic or Slovakia or Slovak Republic or Djibouti or French Somaliland or Dominica or Dominican Republic or East Timor or East Timur or Timor Leste or Ecuador or Egypt* or United Arab Republic or El Salvador or Eritrea or Estonia* or Ethiopia* or Fiji or Gabon or Gabonese Republic or Gambia or Gaza or Georgia or Georgian or Ghana or Gold Coast or Greece or Grenada or Grenadines or Guatemala or Guinea or Guam or Guiana or Guyana or Haiti* or Honduras or Hungary or India* or Maldiv* or Indonesia* or Iran* or Iraq* or Isle of Man or Jamaica* or Jordan* or Kazakhstan or Kazakh or Kenya* or Kiribati or Korea* or Kosovo or Kyrgyzstan* or Kirghizia or Kyrgyz Republic or Kirghiz or Kirgizstan or Lao PDR or Laos or Latvia* or Lebanon or Lebanese or Lesotho or Basutoland or Liberia or Libya* or Lithuania* or Macedonia* or Madagascar or Malagasy Republic or Malaysia* or Malaya or Malay or Sabah or Sarawak or Malawi or Nyasaland or Mali or Malta or Marshall Islands or Mauritania or Mauritius or Agalega Islands or Mexic* or Micronesia or Middle East or Moldova or Moldovia or Moldovian or Mongolia* or Montenegro or Morocco or Ifni or Mozambique or Myanmar or Myanma or Burma or Namibia or Nepal* or Netherlands Antilles or New Caledonia or Nicaragua or Niger or Nigeria* or Northern Mariana Islands or Oman or Muscat or Pakistan or Palau or Palestine or Panama or Paraguay or Peru* or Philippines or Philipines or Phillipines or Phillippines or Poland or Portugal or Principe or Puerto Rico or Romania* or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or Saint Kitts or St Kitts or Nevis or Saint Lucia or St Lucia or Saint Vincent or St Vincent or Grenadines or Samoa* or Samoan Islands or Navigator Island or Navigator Islands or Sao Tome or Saudi Arabia or Senegal or Serbia* or Montenegro or Seychelles or Sierra Leone or Slovenia or Sri Lanka* or Ceylon or Solomon Islands or Somalia* or South Africa* or Sudan* or Suriname or Surinam or Swaziland or Syria or Tajikistan or Tadzhikistan or Tadjikistan or Tadzhik or Tanzania* or Thailand or Thai or Togo or Togolese Republic or Tonga or Trinidad or Tobago or Tunisia* or Turk* or Turkmenistan or Turkmen or Tuvalu or Uganda* or Ukrain* or Uruguay or USSR or Soviet Union or Union of Soviet Socialist Republics or Uzbekistan or Uzbek or Vanuatu or New

Hebrides or Venezuela or Vietnam* or Viet Nam* or West Bank or Yemen* or Yugoslavia or Zambia* or Zimbabwe* or Rhodesia*).hw,kf,ti,ab,cp.

14. 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13

15. 4 and 14

Appendix B- Study Quality Assessment

Authors and year of publication*	Random sample or whole population	Unbiased sampling frame	Adequate sample size (>300 participants)	Used standard measures	Outcomes measured by unbiased assessors	Adequate response rate (70%), refusers described	Confidence interval (CI) for prevalence, subgroup analysis	Study subjects are described	Risk of bias assessment
Tribess et al, 2012[1]	√	×	√	√	×	√,√	×,√	√	5.5
De Andrade et al, 2013[2]	√	√	√	√	×	×,×	×,√	√	5.5
Júnior et al, 2014[3]	√	N/A	×	√	×	√,√	×,√	√	4.5
Pegorari et al, 2014[4]	√	×	√	√	√	√,√	×,√	√	6.5
Corona et al, 2015[5]	√	√	√	√	√	√,×	×,√	√	7.0
Santos et al, 2015[6]	×	×	×	√	√	√,×	×,√	√	4.0
Closs et al, 2016[7]	√	√	√	√	√	×,×	√,√	√	7.0
Mello et al, 2017[8]	√	√	×	√	√	√,×	×,√	√	6.0
de Albuquerque Sousa et al, 2012[9]	√	√	√	√	√	√,×	×,√	√	7.0
dos Santos Amaral et al, 2013[10]	×	×	√	√	√	√,×	×,×	√	4.5
Moreira et al, 2013[11]	√	×	√	√	×	√,√	√,×	√	5.5
Neri et al, 2013[12]	√	√	√	√	√	×,×	×,√	√	6.5
Vieira et al, 2013[13]	√	√	√	√	×	×,√	×,×	√	5.5
Ricci et al, 2014[14]	√	√	√	√	√	√,√	×,√	√	7.5
Silveira et al, 2015[15]	√	√	×	√	×	×,×	×,×	√	4.0
Calado et al, 2016[16]	√	√	√	√	√	√,×	×,√	√	7.0
Augusti et al, 2017[17]	√	√	√	√	√	√,×	×,√	√	7.0
Ferriolli et al, 2017[18]	√	×	√	√	×	√,×	×,√	√	5.0
Grden et al, 2017[19]	√	√	×	√	√	√,×	×,√	√	6.0
Ocampo-Chaparro et al, 2013[20]	√	√	√	√	√	√,×	×,√	√	7.0

Authors and year of publication*	Random sample or whole population	Unbiased sampling frame	Adequate sample size (>300 participants)	Used standard measures	Outcomes measured by unbiased assessors	Adequate response rate (70%), refusers described	Confidence interval (CI) for prevalence, subgroup analysis	Study subjects are described	Risk of bias assessment
Curcio et al, 2014[21]	×	×	√	√	√	×,×	×,√	√	4.5
Samper-Ternent et al, 2016[22]	√	×	√	√	√	×,√	×,√	√	6.0
Garcia-Pena et al, 2016[23]	√	√	√	√	√	√,√	×,√	√	7.5
Sanchez-Garcia et al, 2017[24]	√	√	√	√	√	√,×	×,√	√	7.0
Moreno-Tamayo et al, 2017[25]	√	√	√	√	×	√,√	×,√	√	6.5
Chen et al, 2015[26]	×	×	√	√	√	×,√	×,√	√	5.0
Wu et al ,2017[27]	√	√	√	√	√	√,×	√,√	√	7.5
Dong et al, 2017[28]	√	√	√	√	√	×,×	×,×	√	6.0
Wang et al, 2015[29]	×	×	√	√	√	×, ×	×,√	√	4.5
Badrasawi et al, 2017[30]	√	√	√	√	√	√,√	×,√	√	7.5
Kashikar et al, 2016[31]	√	√	×	√	√	√,√	×,√	√	6.5
Gurina et al, 2011[32]	√	√	√	√	√	×,√	×,√	√	7.0
Alvarado et al, 2008[33]	√	√	√	√	×	√,×	×,√	√	6.0
Aguilar-Navarro et al, 2015[34]	√	√	√	√	√	×,×	×,√	√	6.5
Avila-Funes et al, 2016[35]	√	√	√	√	√	√,√	×,√	√	7.5
Sanchez-Garcia et al, 2014[36]	√	√	√	√	√	N/A	×,√	√	6.5
Akin et al, 2015[37]	√	√	√	√	×	×, ×	×,√	√	5.5
Zhu et al, 2016[38]	√	√	√	√	√	√, √	×, ×	√	7.0
Jotheeswaran et al, 2015[39]	√	N/A	√	√	√	√,×	×,×	√	5.5
Fhon et al, 2012[40]	√	√	×	√	√	√,×	×,√	√	6.0
Agreli et al, 2013[41]	√	√	×	√	×	√,×	×,√	√	5.0
Duarte et al, 2013[42]	√	×	×	√	×	√,×	×,×	√	3.5

Authors and year of publication*	Random sample or whole population	Unbiased sampling frame	Adequate sample size (>300 participants)	Used standard measures	Outcomes measured by unbiased assessors	Adequate response rate (70%), refusers described	Confidence interval (CI) for prevalence, subgroup analysis	Study subjects are described	Risk of bias assessment
Del Brutto et al, 2016[43]	√	N/A	√	√	×	√,√	×,√	√	5.5
Fabricio-Wehbe et al, 2009[44]	√	√	×	√	√	×,×	×,√	√	5.5
Carneiro et al, 2016[45]	√	√	√	√	√	×,×	×,√	√	6.5
Bennett et al, 2013[46]	×	×	√	√	√	×, ×	×,√	√	4.5
Woo et al, 2015[47]	√	√	√	√	√	×, ×	×,√	√	6.5
Hao et al, 2016[48]	√	√	√	√	√	×, ×	√,√	√	7.0
Sathasivam et al, 2015[49]	√	√	√	√	×	√,×	×,√	√	6.0
García-González et al, 2009[50]	√	√	√	√	√	×,×	×,√	√	6.5
Perez-Zepeda et al, 2016[51]	√	√	√	√	√	√,×	×,×	√	6.5
de Leon Gonzalez, 2015[52]	√	×	√	√	×	×,×	×,√	√	4.5
Rosero-Bixby et al, 2009[53]	√	√	√	√	√	×,√	×,√	√	7.0
Galbán et al, 2009[54]	×	×	√	√	×	√,×	×,√	√	4.0
Boulos et al, 2016[55]	√	√	√	√	√	√,×	×,√	√	7.0
Gray et al, 2017[56]	√	√	√	√	√	×,×	×,√	√	6.5
Parentoni et al, 2013[57]	×	×	×	√	×	√,×	×,√	√	3.0
Bastone et al, 2015[58]	×	×	×	√	×	√,√	×,×	√	3.0
Cakmur et al, 2015[59]	×	×	×	√	×	√,×	×, ×	√	2.5
Sampaio et al, 2015[60]	×	×	×	√	×	×,×	×,×	√	2.0
Zainuddin et al, 2017[61]	×	×	×	√	×	×,×	×,√	√	2.5

√- Criteria is satisfied ×- Criteria is not satisfied/ not documented N/A- Not applicable

Appendix C: Characteristics of the studies included in the systematic review of prevalence of frailty and pre-frailty

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants' mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									frailty	pre-frailty		
Tribess et al, 2012[1]	Brazil	Population Study of Physical Activity and Aging (EPAFE), City of Uberaba, Minas Gerais Conducted from May to August 2010	Cross sectional study	622	65	≥ 60 (71.0±7.7) 60-96	Random sampling	Fried Phenotype ǂ	19.9	49.8	Socio-demographic characteristics of the elderly in this study are similar to those reported in surveys in Latin America indicates the potential generalization of the present results to other populations.	The measurements of self-perception may have been influenced by the low educational level of participants and their motivational aspects.
De Andrade et al, 2013[2]	Brazil	SABE study (Wave 2-2006) Survivors from baseline study (2000) and new participants of the second wave São Paulo	Cross sectional study with SABE data	1374	59.7	≥ 60	Cluster sampling	Fried Phenotype ǂ	8.5	40.7	Use of large representative sample of community dwelling elderly increases the generalizability of results. Frailty has measured using well defined method.	Use of self-reported data on physical activities may introduce biases that are difficult to control.
Júnior et al, 2014[3]	Brazil	Epidemiological study titled Nutritional status, risk behaviours and health conditions of the elderly people of Lafaiete Coutinho-BA Urban area	Cross sectional study	286	54.2	≥ 60	Census of all older adults in the area	Fried Phenotype ǂ	23.8	58.7	-	Some instruments used in the study required subjective or self-reported information that can be lead to memory bias.
Pegorari et al, 2014[4]	Brazil	Urban area of the city of Uberaba, MG	Cross sectional observational and analytical household survey	958	64.4	≥ 60 (73.7±6.7)	Stratified proportional sampling	Fried Phenotype ǂ	12.8	54.5	Results of the study contribute to deepen knowledge of frailty syndrome among Brazilian elderly	-

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants' mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									frailty	pre-frailty		
Pegorari et al, 2014[4] cont.											individuals and support planning and implementation of interventions and care actions.	
Corona et al, 2015[5]	Brazil	SABE study (Wave 3-2010), Survivors from baseline (2000) and second wave (2006) and new participants of the third wave São Paulo	Cross sectional population based study	1171	65.0	≥ 60	Probabilistic sampling	Fried Phenotype ǂ	11.3	50.6	Large population base cohort, with a representative sample of community dwelling older adults from the largest city in Brazil.	-
Santos et al, 2015[6]	Brazil	Database called "Identifying the health disease process enrolled population at the Family Health Units" Pau Ferro, municipality of Jequie/BA Conducted from May to November 2013	Observational cross sectional study	136	75.5	≥60 (72.3±8.4) 60-101	-	Fried Phenotype ǂ	16.9	61.8	-	-
Closs et al, 2016[7]	Brazil	Multidimensional Study of the Elderly in the Family Health Strategy (EMI-SUS) Conducted from March 2011 to December 2012	Cross-sectional study	521	64.3	≥60 (68.5 ± 6.8)		Fried Phenotype ǂ	21.5 (17.97-25.03)	51.1 (46.81-55.39)	-	The cross-sectional design of the study. Access to the study by immobile or bedridden elderly people was limited as the frailty and geriatric syndromes evaluations were performed in an outpatient setting and not in their own homes.

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants' mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									frailty	pre-frailty		
Mello et al, 2017[8]	Brazil	Survey on Conditions of Health and Use of Health Services in the Territory of Manguinhos, Rio de Janeiro Municipality Manguinhos neighborhood of Rio de Janeiro	Cross-sectional study	137	67.9	≥60 (70.2±7.4)	All the older adults identified by the Manguinhos-Health Survey	Fried Phenotype ǂ	12.4	61.3	-	Sample size is small and it represents around 10% of the population of this age group in the region. It is not possible to establish a cause and effect relationship. The grip strength, physical activity and gait speed, have been adapted to fit the local reality of the research, which may lead to some differences when comparing with the results of other studies.
de Albuquerque Sousa et al, 2012[9]	Brazil	FIBRA- urban zone of Santa Cruz city	Cross sectional study	391	61.4	≥ 65 (74.0±6.5) 65-96	Random sampling	Fried Phenotype ǂ	17.1	60.1	-	Adapted version of the Minnesota Questionnaire of Physical Activities and Leisure was used in this study as original questionnaire did not match with Brazilian cultural context. The used cut-off point (20th percentile) may be underestimating the physical activity level.

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants' mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									frailty	pre-frailty		
dos Santos Amaral et al, 2013[10]	Brazil	This study is a part of a project titled "Allostatic load, frailty and functionality in the elderly" Neighbourhood Rocas, Natal	Analytical observational cross sectional study	295	67.3	≥ 65 (74.3±6.9) 65-100	-	Fried Phenotype ǂ	18.6	55.3	Sample is representative. Low percentage of refusals.	-
Moreira et al, 2013[11]	Brazil	FIBRA- Northern area of the city of Rio de Janeiro Conducted from January 2009 to January 2010	Cross sectional descriptive study	754	66.9	≥ 65 (76.6±6.9)	Inverse random sampling stratified by gender and age	Fried Phenotype ǂ	9.5	47.5	-	An adapted version of Minnesota Questionnaire of Physical Activities and Leisure was used in this study. However, it is also problematic as reference activities in the questionnaire are atypical in Brazilian culture. This may lead to errors in estimating the weekly caloric expenditure.
Neri et al, 2013[12]	Brazil	FIBRA Seven cities		3413	67.6	≥ 65	Probability sampling	Fried Phenotype ǂ	9.0	51.9	Measures were taken to avoid the systematic distortions of data. i.e. encouraging participation of the elderly, standardization of procedures, instruments and equipment, comprehensive training of staff in all locations, procedures were adopted to ensure greater reliability of data entered in the electronic	More female representation in the study sample limited the generalizability of results. Loss of information during the data collection could affect the reliability of data. Study participation in Ivoti was lower than expected due to the problems of time and transport.
		Belem		720	69.5				10.8	48.2		
		Parnaiba		431		73.9			9.7	55.5		
		Campina Grande		395	70.1				8.9	51.4		
		Pocos de Caldas		388	61.4				9.3	53.4		
		Ermelino Matarazzo, Sao Paulo		384	67.2				8.1	54.9		
		Campinas		898	69.3				7.7	52.2		
		Ivoti		197	70.1				8.6	47.7		

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants' mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI frailty	Prevalence (%), 95% CI pre-frailty	Study strengths reported by authors	Study limitations reported by authors
Neri et al, 2013[12] cont.											banks.	Selection of older people without cognitive impairment and required to attend to the data collection site by their own might have introduced the survival bias into the study.
Vieira et al, 2013[13]	Brazil	FIBRA-Belo Horizonte, Minas Gerais State Conducted from December 2008 to September 2009	Population based cross sectional study	601	66.2	≥ 65 (74.3±6.4)	Probability sampling	Fried Phenotype ǂ	8.7	46.3	-	Phenotype limits the evaluation of possible frail elderly with cognitive impairment, gait restriction, severe motor sequale. Use of Minnesota Questionnaire of Physical Activities and Leisure is not fitting with the Brazilian cultural context.
Ricci et al, 2014[14]	Brazil	FIBRA- Barueri and Cuiaba urban municipalities	Cross sectional population based study	761	64.3	≥ 65 (71.9±5.9)	Census of older adults in 27 census tracts	Fried Phenotype ǂ	9.7	48.0	-	The phenotype used in the study basically comprised of physical frailty and not include other markers such as cognitive decline and psychosocial aspects.
Silveira et al, 2015[15]	Brazil	Uberaba, Minas Gerais Conducted from July to October 2011	Analytical observational cross sectional study	54	59.3	≥ 65 (72.9±6.0)	Random sampling	Fried Phenotype ǂ	11.1	46.2	-	-

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants'/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI frailty	pre-frailty	Study strengths reported by authors	Study limitations reported by authors
Calado et al, 2016[16]	Brazil	FIBRA-Ribeirão Preto, state of São Paulo	Cross sectional study	385	64.7	≥65 (73.9 ± 6.5)	Random sampling	Fried Phenotype ǂ	9.1	49.6	-	Cross-sectional nature of the study does not allow any temporal relationship between the variables to be established. And also, this design is subject to survival bias, which could lead to underestimation of the associations observed. Study has excluded patients who were already known to be dependent. This may have affect the prevalence of frailty.
Augusti et al, 2017[17]	Brazil	Amparo, in the state of São Paulo	Cross-sectional study	306	60.2	≥65 (72.6± 5.7)	Random sampling	Fried Phenotype ǂ	21.5	71.6	-	-
Ferriolli et al, 2017[18]	Brazil	Recife	Cross-sectional study	556	70.6	≥ 65 (73.9±6.8)	Probability sampling	Fried Phenotype ǂ	12.1	66.9	-	Cannot establish the causal nexus between the studied variables and frailty due to the cross-sectional design. The method used to assess body composition of older adults is debatable.
		Juiz de Fora		412	69.6	≥ 65 (74.2±6.6)			15.5	63.1		
		Fortaleza		481	67.9	≥ 65 (74.8±7.2)			10.4	63.6		
Grden et al, 2017[19]	Brazil	Area covered by three basic health units belong to the Boa Vista Sanitary District,	Cross-sectional study	243	66.3	≥80 (84.4±3.8)	Proportional stratified sampling	Fried Phenotype ǂ	14.8	63.8	-	Cross-sectional design is a limiting factor in evaluating cause and effect relationships.

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants'/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									frailty	pre-frailty		
Grden et al, 2017[19] cont.		in the city of Curitiba, Paraná Conducted from January 2013 to September 2015										This sample only represents the local community, and therefore the results cannot be extrapolated to other territories.
Ocampo-Chaparro et al, 2013[20]	Colombia	Commune 18, City of Cali (urban area) Conducted in 2009	Population based cross sectional study	314	64.3	≥ 60	Single stage cluster sampling	Fried Phenotype ǂ	12.7	71.3	-	The study was conducted in a localized area and not in the entire city of Cali. And also study population did not include rural, institutionalized adults. Hence it limited the external validity of the findings
Curcio et al, 2014[21]	Colombia	Four villages located in the coffee growing zone of the Andese mountains, (rural area) Conducted in 2005	Cross sectional study	1878	52.2	≥ 60 (70.9±7.4)	Voluntary participation	Fried Phenotype ǂ	12.2	53.0	Sample size is large. Used comprehensive set of measurements. First study that measured the prevalence of frailty in older adults living in rural areas in the Latin American and Caribbean. Established the relationship between frailty, higher prevalence of chronic conditions and disabilities among elderly people in Latin America.	-

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants'/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI frailty	Prevalence (%), 95% CI pre-frailty	Study strengths reported by authors	Study limitations reported by authors
Samper-Ternent et al, 2016[22]	Colombia	Data from Salud Bienestar y Enve-Jecimiento (SABE) Bogota study Both urban and rural areas of Bogota Data collected in 2012	Cross sectional survey	1442	61.0	≥ 60 (70.7±7.7)	Probabilistic sampling by clusters with block stratification	Fried Phenotype ǂ	9.4	52.4	First population based study of adults over 60 in Colombia to explore the conditions that affect their health and quality of life. Study followed the international guidelines previously used in other capital cities in Latin America and was modified to fit the social and historical situation of Colombia. Used constructs validated in similar populations for assessed frailty previously.	Modification to the frailty phenotype definition could introduce bias to the analysis. Large percentage of cohort from the current study was excluded as there was missing data for construction of frailty and sarcopenia variables (n=558). Excluded individuals were significantly different from study population which could introduce bias to the study. Some data are self-reported so recall bias could affect the results.
Garcia-Pena et al, 2016[23]	Mexico	Mexican Health and Aging Study (MHAS) Wave 3 Conducted in 2012	Secondary analysis	1108	54.6	≥ 60 (69.8±7.6)	-	Fried Phenotype ǂ Frailty index-32 variables	24.9 27.5	61.0 -	Large comprehensive dataset. Used previously validated frailty classifying tools. (Fried phenotype and frailty index)	The cut-off value to define frailty by frailty index was arbitrary although it was based on previous research. Included 32 deficits in frailty index as self-rated hearing and abdominal pain were not available in the 2012 wave.

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants'/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI frailty	Prevalence (%), 95% CI pre-frailty	Study strengths reported by authors	Study limitations reported by authors
Garcia-Pena et al, 2016[23] cont.												Categorization of physical activity in Fried phenotype was different from previous reports.
Sánchez-García et al, 2017[24]	Mexico	Baseline assessment ''Cohort of Obesity, Sarcopenia and Frailty of Older Mexican Adults'' (COSFOMA) Mexico city Conducted from April to September 2014	Cross-sectional analysis	1252	59.9	≥60 (68.5 ± 7.2)	Random sampling	Fried Phenotype ǂ	11.2	50.3	-	Cross-sectional design does not establish a causal relationship between frailty and quality of life in the elderly.
Moreno-Tamayo et al, 2017[25]	Mexico	Rural Frailty Study (Prospective study) Follow up data collected in 2013	Cross-sectional study	657	52.9	≥70 (76.3 ± 3.3)	Random sampling	Fried Phenotype ǂ	11.9	51.9	Use of Fried's phenotype frailty assessment.	Cross-sectional design does not allow for drawing conclusions about the direction of causality.
Chen et al, 2015[26]	China	Data from a cross sectional study, Comprehensive Geriatric Assessment and Health Care Service Study Chengdu and Suining, Southwest China Conducted from October 2010 to August 2012	Cross sectional study	604	57.9	≥ 60 (70.6±6.8) 60-91	Convenience sampling	Fried Phenotype ǂ	12.7	56.5	-	Data must be interpreted with caution. The number of the participants was below 1000, although the study population was representative of the 60+ year old community dwelling adults in this specific area. The information about disease and some of the frailty items measurements were taken through

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants'/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI frailty	pre-frailty	Study strengths reported by authors	Study limitations reported by authors
Chen et al, 2015[26] cont.												self-reported questionnaires. Older people who refused to participate had lower level of functionality which might have nonresponse bias or selection bias. Present study has only included Han people. Therefore, conclusions might not generalizable to other ethnic populations.
Wu et al, 2017[27]	China	The China Health and Retirement Longitudinal Study 28 provinces in China (2011-2012)	Baseline survey of an ongoing longitudinal study	5290	49.0	≥60 (69.2±7.0)	Multistage probability sampling	Fried Phenotype ǂ	6.3	51.3	First study that utilized the Fried phenotype of frailty scale to examine prevalence of frailty in a nationally representative sample of noninstitutionalized Chinese adults aged 60 years or older. Constructed cut-points for define five physical frailty phenotype criteria in Chinese elders. First study that examined the regional variation	This study does not include the nursing home residents. Therefore, there is a possibility of underestimating the prevalence of frailty among the entire Chinese elderly population. However, it is worthy to note that only 1.5% of older adults live in nursing homes in China. All five frailty components were only measured once; these measures may vary over time.

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants'/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI frailty	pre-frailty	Study strengths reported by authors	Study limitations reported by authors
Wu et al, 2017[27] cont.											in frailty in mainland China. First study that investigated the association of biomarkers with frailty among Chinese older adults.	Unable to establish a causal association of chronic conditions and disability with frailty because the study is a cross-sectional analysis
Dong et al, 2017[28]	China	Jinan City, Shandong Province, Eastern China Conducted from July to December 2016	Cross-sectional study	1188 1215	69.1 69.5	≥60 (69.5±6.7) 60-95	Multistage stratified sampling	Fried Phenotype ǂ	3.9 17.4	45.9 21.5	-	Generalizability of the results should be treated cautiously because the participants were just from one city in China.
Wang et al, 2015[29]	China	Changsha city and its surrounding area Conducted from August 2012 to August 2014	-	316	48.1	≥ 65 (75.6±4.8) (men) (76.9±5.2) (women)	-	Fried Phenotype ǂ	14.2	49.1	Participants were recruited from a community based elderly population.	Individuals were originally excluded if unable to walk without assistance of another person, or their renal function and liver function is abnormal, or their heart function classification is grades III and IV according to New York Heart Association standard. This may have biased the results towards an underestimation of the risk of frailty associated with sarcoosteopenia
Badrasawi et al, 2017[30]	Malaysia	Neuroprotective model for healthy longevity among Malaysian older adults	Part of a longitudinal study	473	55.6	≥60 (68.2±5.8)	Multistage random sampling	Fried Phenotype ǂ	8.9	61.7	-	Use of original Fried's cut-off values for grip strength and gait speed.

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants'/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI frailty	pre-frailty	Study strengths reported by authors	Study limitations reported by authors
Badrasawi et al, 2017[30] cont.		Conducted from 5th July 2013 to 22nd February 2014										Causal relationships should be interpreted with caution since the study is cross-sectional.
Kashikar et al, 2016[31]	India	Warje-Karvenagar, Pune city	Cross-sectional study	250	50.0	≥65 (73.9± 6.4)	Multi stage random sampling	Fried Phenotype ǂ	26.0	63.6	-	-
Gurina et al, 2011[32]	Russia	Data from "Crystal" prospective cohort study Kolpino district of St. Petersburg Conducted from March to December 2009	Cross sectional study	611	71.7	≥ 65 (75.1±5.9)	Random sample stratified by age	Fried Phenotype ǂ (whole study population)	21.1	63.0	Analysis provides a better understanding of the health status of older adults in Russia.	Cross sectional analysis is not adequate for frailty analysis as this phenotype is more dynamic than static. The prognostic significance of the different frailty indicators and models will become clearer after the follow up data are analysed. The tested frailty models were modified by using proxies for some of the original indicators. Findings can be generalized to the whole population of St. Petersburg only with caution, the Kolpino district represents one of the 18 districts of the city.
								Fried Phenotype ǂ (adjusted for MMSE score <18, Parkinson's disease, and stroke)	17.9	65.5		
								Steverink–Slaets model, Groningen Frailty Indicator	32.6	24.7		
								Extended Puts model	43.9	42.9		

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants'/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI frailty	pre-frailty	Study strengths reported by authors	Study limitations reported by authors
Alvarado et al, 2008[33]	Barbados Brazil Chile Cuba Mexico	Health, Wellbeing and Ageing study (SABE) study Conducted from 1999 to 2000	Multi centric cross sectional study	7334	-	≥ 60	Multi-staged sampling	Fried phenotype §	-	-	-	Operationalization of Fried phenotypic criteria is different from the original Cardiovascular Health Study (CHS) of Fried et al, 2001. And also, possible background risk differences (cultural and other social biological factors) may limit the comparison of this study results with other studies.
		Bridgetown, Barbados		1446	61.1				26.7	54.4		
		São Paulo, Brazil		1879	59.3				40.6	48.8		
		Santiago de Chile, Chile		1220	66.1				42.6	51.4		
		Havana, Cuba		1726	62.7				39.0	51.6		
		Mexico, DC, Mexico		1063	60.4				39.5	49.0		
Aguilar-Navarro et al, 2015[34]	Mexico	Subset from Mexican Health and Aging Study (MHAS) Wave 1 Conducted in summer of 2001	Longitudinal study (cross sectional data)	5644	53.6	≥ 60 (68.7±6.9)	Random sample	Fried Phenotype §	37.2	51.3	Population based design. Large sample size.	Operationalization of Fried phenotypic criteria is different from the original CHS of Fried et al, 2001. The original metrics were not available in the MHAS cohort. It could results possible overestimation of prevalence of frailty.
Avila-Funes et al, 2016[35]	Mexico	Subset of Mexican Study of Nutritional and Psychosocial Markers of Frailty (prospective cohort study) Coyoacán cohort Conducted from April 2008 to July 2009	Cross-sectional study using the data of prospective cohort study	927	54.9	≥ 70 Median age-76.5 70.3-104.4	Random sampling stratified by age and sex	Fried Phenotype §	14.1	37.3	Population based sample, from a cohort specifically designed to identify the correlates of frailty.	Recruitment was carried out in only one district of Mexico city, therefore these results might not be representative of rural areas of Mexico.

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									frailty	pre-frailty		
Sanchez-Garcia et al, 2014[36]	Mexico	Data from Study on Aging and Dementia in Mexico (SADEM) Conducted from September 2009 to March 2010	Not mentioned in the article	1933	58.0	≥ 60 70.1±7.1 (women) 71.7±7.4 (men)	Random sample from original database	Fried Phenotype with 4 criteria	15.7	33.3	-	Definitions used to evaluate frailty and pre-frailty.
Akin et al, 2015[37]	Turkey	Kayseri (urban area) Data of Kayseri Elderly Health Study (KEHES) Kayseri Conducted from August to December 2013	Cross sectional population based study	848 897	50.6	≥ 60 (71.5±5.6)	Stratified random sampling and any Individual older than 60 years who requested to participate was also included.	Fried Phenotype with 4 criteria FRAIL scale	27.8 10.0	34.8 45.6	-	Absence of physical activity in this study may have under or overestimated the prevalence of frailty. Relatively small sample size of elderly participants aged ≥ 85 years.
Zhu et al, 2016[38]	China	Cross sectional data from the ageing arm of the Rugao Longevity and Ageing Study 31 villages in Jiang'an township, Rugao city Conducted from November 2014 to December 2014	-	1478	53.0	≥ 70 (75.3±3.9) 70-84	Random sampling	Frailty phenotype with 4 criteria	12.0	42.9	Representativeness of the study participants increases the generalisability of the findings. The study participants were randomly selected with a higher participant rate (91.2%) representing approximately 16% of the elderly in Jiang'an township. The Findings from such a representative population based sample might be generalisable to most elderly people in China.	-

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI frailty	pre-frailty	Study strengths reported by authors	Study limitations reported by authors
Jotheeswaran et al, 2015[39]	China Mexico Peru Cuba Dominican Republic Venezuela India	10/66 Dementia Research Group's (10/66 DRG) population based studies of ageing and dementia in LMICs Data collected between 2003 and 2007	Cross sectional survey	12373	62.3	≥ 65 (74.1±7.0)	Census	Fried Phenotype with 4 criteria	17.5	-	Study was conducted with large population based cohorts in Latin America, India and China allowing to assess the consistency or cultural specificity of the observed associations. Study design was prospective, limiting information bias with modest attrition. Walking speed, under nutrition and cognitive impairment were measured objectively. Visual and auditory impairment have been assessed by objective testing.	Hand grip strength was not measured in this study. Hence physical frailty construct is only an approximation to the original Fried definition. The impact of this omission is difficult to assess.
								Multi dimentional frailty model	29.1	-		
								Fried Phenotype with 4 criteria				
		China (Urban)		989	56.6	(74.1±6.3)			7.8	-		
		China (Rural)		1002	55.5	(72.4±6.0)			8.7	-		
		Cuba (Urban)		2637	65.0	(75.2±7.1)			21.0	-		
		Dominican Republic (Urban)		1706	66.3	(75.4±7.6)			34.6	-		
		India (Urban)		748	57.2	(71.4±6.1)			11.4	-		
		Mexico (Urban)		909	66.5	(74.4±6.6)			10.1	-		
		Mexico (Rural)		933	60.9	(74.1±6.6)			8.5	-		
		Peru (Urban)		1245	64.7	(75.0±7.4)			25.9	-		
		Peru (Rural)		507	53.2	(74.1±7.3)			17.2	-		
		Venezuela (Urban)		1697	63.2	(72.3±6.8)			11.0	-		
		China (Urban)		989	56.6	(74.1±6.3)		Multi dimentional frailty model	11.3	-		
		China (Rural)		1002	55.5	(72.4±6.0)			22.5	-		
		Cuba (Urban)		2637	65.0	(75.2±7.1)			33.7	-		
		Dominican Republic (Urban)		1706	66.3	(75.4±7.6)			47.8	-		
		India (Urban)		748	57.2	(71.4±6.1)			26.1	-		
		Mexico (Urban)		909	66.5	(74.4±6.6)			22.9	-		
		Mexico (Rural)		933	60.9	(74.1±6.6)			36.2	-		
		Peru (Urban)		1245	64.7	(75.0±7.4)			28.2	-		
		Peru (Rural)		507	53.2	(74.1±7.3)			25.6	-		
		Venezuela (Urban)		1697	63.2	(72.3±6.8)			20.0	-		

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI frailty	pre-frailty	Study strengths reported by authors	Study limitations reported by authors
Fhon et al, 2012[40]	Brazil	Municipality of Ribeirao Preto, Sao Paulo Conducted from November 2010 to February 2011	Cross sectional study	240	62.9	≥ 60 (73.5±8.4)	Two stage conglomerate sampling	Edmonton frail scale	39.2	24.6	-	-
Agreli et al, 2013[41]	Brazil	Embu, City in metropolitan region of Sao Paulo Conducted from June to July 2010	Observational descriptive cross sectional study	103	62.1	≥ 60 (68.9±7.8) 60-103	Simple random sampling	Edmonton frail scale	30.1	22.3	-	Older adults who did not respond to the clock test could not classify for their degree of frailty.
Duarte et al, 2013[42]	Brazil	This study is a sub project of the survey "Living conditions, health and ageing: a comparative study" City of Joao Pessoa, the state capital of Paraiba Conducted from April to June 2011	Cross sectional study	166	100.0	≥ 60 (73.0±6) 60-96	Two staged cluster sampling	Edmonton frail scale	39.2	21.7	-	-
Del Brutto et al, 2016[43]	Ecuador	Atahualpa, a rural village of costal Ecuador	Cross sectional population based study	298	57.0	≥ 60 (70.0±8.0)	Individuals identified through yearly door-to-door survey	Edmonton frail scale	31.2	22.0	Population based design. Lack of selection bias. Used a reliable instrument to identify frailty.	-
Fabricio-Wehbe et al, 2009[44]	Brazil	Ribeirao Preto, Sao Paulo Conducted from September 2007 to June 2008	-	137	74.5	≥ 65 (75.3±8.0) 65-100	Probabilistic sampling	Edmonton frail scale	31.4	20.4	-	-
Carneiro et al, 2016[45]	Brazil	City of Montes Claros, northern Minas Gerais Conducted from May to July 2013	Cross-sectional study	511	64.0	≥65 (74.0± 7.1)	Two stage cluster sampling	Edmonton frail scale	41.3	-	Representative sample.	Losses or refusals were compensated by adding new older adults. However, more active older adults

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI frailty	pre-frailty	Study strengths reported by authors	Study limitations reported by authors
Carneiro et al, 2016[45] cont.												who were probably without frailty were not found at home during the visits. This can limit the generalizability of the data. This is a cross-sectional study and cannot establish the temporal relationship among the observed associations.
Bennett et al, 2013[46]	China	Longevity Study (CLHLS) 22 provinces of China	Secondary analysis	6300	-	80-99	-	Frailty index 38 deficits	FI≤ 0.05-15.0 0.05< FI≤ 0.15-53.2 0.15< FI≤ 0.25-20.2 0.25< FI≤ 0.35-6.7 0.35< FI≤ 0.45-3.3 FI >0.45-1.6		-	The baseline cohort included 36% centenarians and they have been excluded from the analysis. Hence, results should be interpreted with caution.
Woo et al, 2015[47]	China	Data from Beijing Longitudinal Study of Aging II (BLSA II) Three urban districts (Xuanwu, Xicheng and Dongcheng) and one rural county (Shunyi) from the 18 administrative districts or counties in Beijing Participants were recruited from July to November 2009	-	6320 (urban) 978 (rural)	61.5 57.2	≥ 65 74.6±5.6 (men) 73.8±5.2 (women) (74.8±5.7) (men) (73.9±5.0) (women)	Multistage cluster sampling	Frailty index 34 variables	17.0 5.2	- -	-	-

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age/Age range (years)	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI frailty	pre-frailty	Study strengths reported by authors	Study limitations reported by authors
Hao et al, 2016[48]	China	Data from Project of Longevity and Aging in Dujiangyan Dujiangyan region, Sichuan province	Cross sectional study	767	68.0	≥ 90 (93.7±3.4) 90-108	Based on a census of older people above 90 years	Frailty index 35 variables	61.8	-	Frailty index does not rely on specific set of variables. Hence evaluation of frailty is more feasible.	Data needed to be interpreted with caution. The number of participants who gave the consent is still limited. The study population clearly represent a survivor group.
Sathasivam et al, 2015[49]	Malaysia	Urban district	Multistage cross sectional study	789	59.4	≥ 60 (69.6±7.2)	Multi stage random sampling	Frailty index 40 variables	5.7	67.7	Population based study.	There are no normative values that have been consensually established to date to define severity of frailty levels in Malaysia. Findings cannot be generalised to other ethnic groups from similar middle income countries.
García-González et al, 2009[50]	Mexico	Mexican Health and Aging Study (MHAS) Wave 1	Follow up study	4082	52.5	≥65 (73.0)	Probabilistic sample	Frailty index (FI) -34 variables	5 FI levels .00-.07-17.4 .07-.14-30.8 .14-.21-24.0 .21-.35-21.4 .35-.65-6.5		-	-
Perez-Zepeda et al, 2016[51]	Mexico	Data from nationwide survey representing urban and rural areas, Mexican Survey on Nutrition and Health (ENSANUT), 2012	Cross sectional analysis	7108	54.7	≥ 60 (70.7±8.1)	Multistage stratified sampling	Frailty index-44 variables	45.2	-	-	-

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI		Study strengths reported by authors	Study limitations reported by authors
									frailty	pre-frailty		
de Leon Gonzalez, 2015[52]	Mexico	Mexican Health and Aging Study (MHAS) Wave 1	-	4729	-	≥60	-	FRAIL scale	10.4	44.8	Large sample size of men and women living in the community.	Participants who did not complete the performance measures in the population study, and did not include in the present analysis are expected to be less healthy and more likely to die. This increases the possibility of survival bias.
Rosero-Bixby et al, 2009[53]	Costa-Rica	Costa Rican Study on Longevity and Healthy Aging (CRELES)	-	2704	-	≥ 60	Random sampling	Physical frailty using five physical tests	17.8 (60-79 years 57.0 (80+ years)	- -	-	-
Galban et al, 2009[54]	Cuba	Antonio Maceo, Cerro municipality, Havana, Cuba Data collected in 2005	Observational descriptive cross sectional study	541	58.0	≥ 60	-	Geriatric Functional Assessment Scale was applied to classify the participants to frail and non-frail groups according to Cuban frailty criteria	51.4	-	-	-
Boulos et al, 2016[55]	Lebanon	Rural areas Conducted from March 2011 to 2012	Cross sectional study	1120	50.8	≥ 65 (75.7±7.1)	Multi staged cluster sampling	Study of Osteoporotic Fractures (SOF) frailty index	36.4	30.4	Results may be generalisable to rural Lebanese elderly as study involved large representative sample with high response rate. This is the first study reporting estimates about	First part of questionnaire was based on self-reported information which might be affected by memory and education bias due to educational disparities.

Authors and year of publication*	Country	Data source/study setting/time period	Study design	Effective sample	Female %	Participants/ Mean age	Sampling technique	Frailty assessment method	Prevalence (%), 95% CI frailty	pre-frailty	Study strengths reported by authors	Study limitations reported by authors
Boulos et al, 2016[55] cont.											frailty and associated factors in elderly Lebanese community dwellers. Data collection for frailty was based on a widely used and well validated instrument.	Cognitive impairment might affect the accuracy of the SOF index and underestimate the frailty. Widely used Fried phenotype was not used in this study due to the difficulty of performing the walking test (possible space constraints and lack of standardized conditions in Lebanese rural households.)
Gray et al, 2017[56]	Tanzania	Six villages in the rural Hai District of northern Tanzania	Follow up cohort	941	55.8	≥70 (77.2± 6.4)	Census of selected villages	Brief Frailty Instrument for Tanzania (B-FIT)	4.6	13.4	The screening tool could be administered without the need of any specialist knowledge or training and may be suited for use in low-resource settings.	The B-FIT requires further assessment of its face, content, and constructs validity, and the inclusion of a broader range of items should be considered.

Fried Phenotype ǂ = Fried Phenotype with 5 criteria-weakness and slowness assessed using objective tests

Fried Phenotype § = Fried Phenotype with 5 criteria-weakness and slowness assessed using self-reported questions (subjective)

*References for the tables in appendix B and C are listed at the end of this document.

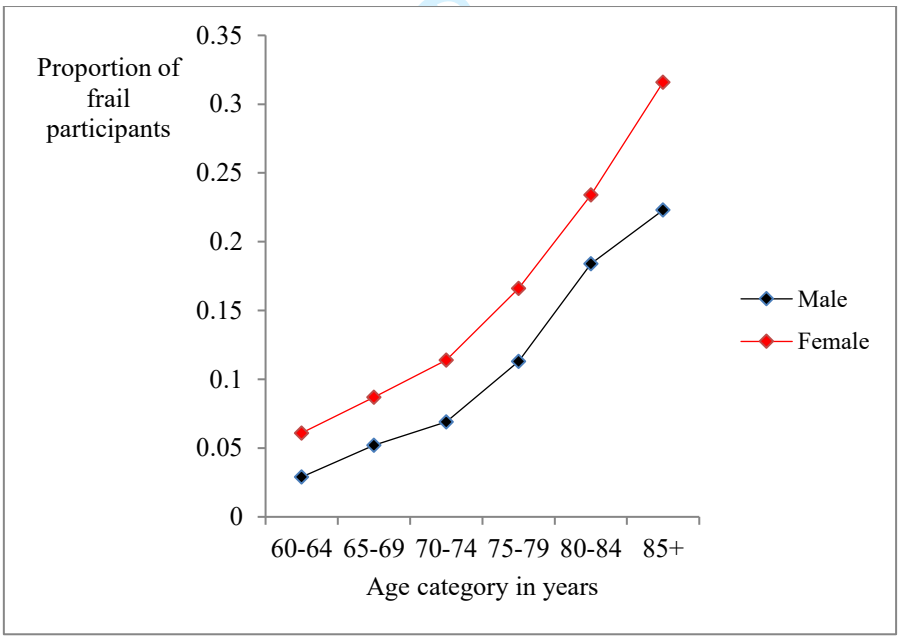
Appendix D: Random effects pooled prevalence of frailty and pre-frailty stratified by frailty assessment method

Frailty assessment method	Number of studies (estimates)	Number of participants	Pooled prevalence (%)	95% CI (%)	Cochran's Q	Degrees of freedom	p value	I^2 (%)
Frailty								
Fried phenotype with 5 criteria-weakness and slowness assessed using objective tests	30 (38)	27623	12.7	10.9-14.5	709.9	37	<0.001	94.8
Fried phenotype with 5 criteria-weakness and slowness assessed using self-reported questions (subjective)	3 (7)	13905	33.8	27.6-40.4	359.1	6	<0.001	98.3
Fried phenotype with only 4 criteria	4 (13)	16632	15.6	11.4-20.3	772.1	12	<0.001	98.4
Edmonton Frail Scale	6 (6)	1455	35.9	31.7-40.2	13.1	5	0.022	61.9
Frailty index	4 (5)	16303	18.0	5.8-35.0	2085.5	4	<0.001	99.8
FRAIL scale	3 (3)	6841	12.4	8.4-17.1	Not computed	2	<0.001	Not computed
Multi-dimensional frailty model	1 (10)	12373	26.9	20.6-33.8	628.8	9	<0.001	98.6
Pre-frailty								
Fried phenotype with 5 criteria-weakness and slowness assessed using objective tests	30 (38)	27623	55.2	53.3-571	360.6	37	<0.001	89.7
Fried phenotype with 5 criteria-weakness and slowness assessed using self-reported questions (subjective)	3 (7)	13905	49.2	46.0-52.4	79.5	6	<0.001	92.5
Fried phenotype with only 4 criteria	3 (3)	4259	37.0	30.9-43.3	Not computed	2	Not computed	Not computed
Edmonton Frail Scale	5 (5)	944	22.3	19.7-25.0	1.0	4	0.907	0.0
FRAIL scale	3 (3)	6841	38.9	27.6-50.7	Not computed	2	Not computed	Not computed

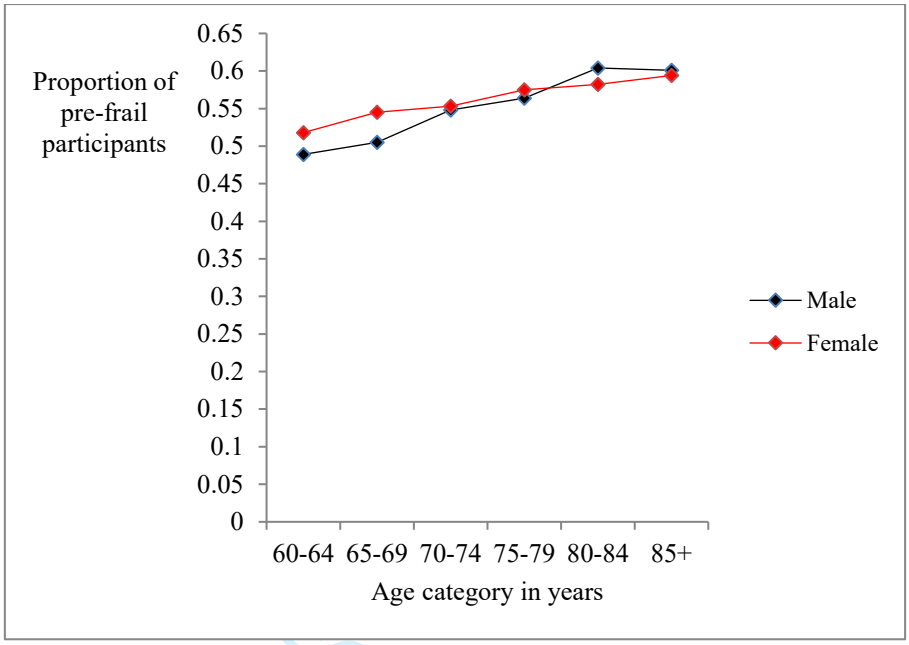
Appendix E: Pooled prevalence of frailty and pre-frailty by five years age categories for studies used Fried phenotype with 5 criteria where weakness and slowness assessed using objective tests

Age category	Number of studies	Number of participants	Pooled prevalence (%)	95% CI (%)	Cochran's Q	Degrees of freedom	p value	I^2 (%)
Frailty								
60-64	13	4386	6.2	4.0-8.8	100.4	12	<0.001	88.1
65-69	21	6437	8.2	6.3-10.3	138.2	20	<0.001	85.5
70-74	22	5666	10.3	8.2-12.6	136.4	21	<0.001	84.6
75-79	22	4121	15.4	12.6-18.4	115.6	21	<0.001	81.3
80-84	22	2329	22.6	18.5-26.9	97.7	21	<0.001	78.5
85+	22	1249	29.8	25.6-34.2	42.1	21	0.004	50.1
Pre-frailty								
60-64	13	4386	52.3	47.9-56.8	86.7	12	<0.001	86.2
65-69	21	6437	53.5	49.8-57.1	148.1	20	<0.001	86.5
70-74	22	5666	54.8	51.6-57.9	100.6	21	<0.001	79.1
75-79	22	4121	57.0	55.0-59.1	30.6	21	0.080	31.5
80-84	22	2329	57.9	55.5-60.3	25.8	21	0.213	18.7
85+	22	1249	59.3	55.9-62.6	25.4	21	0.229	17.4

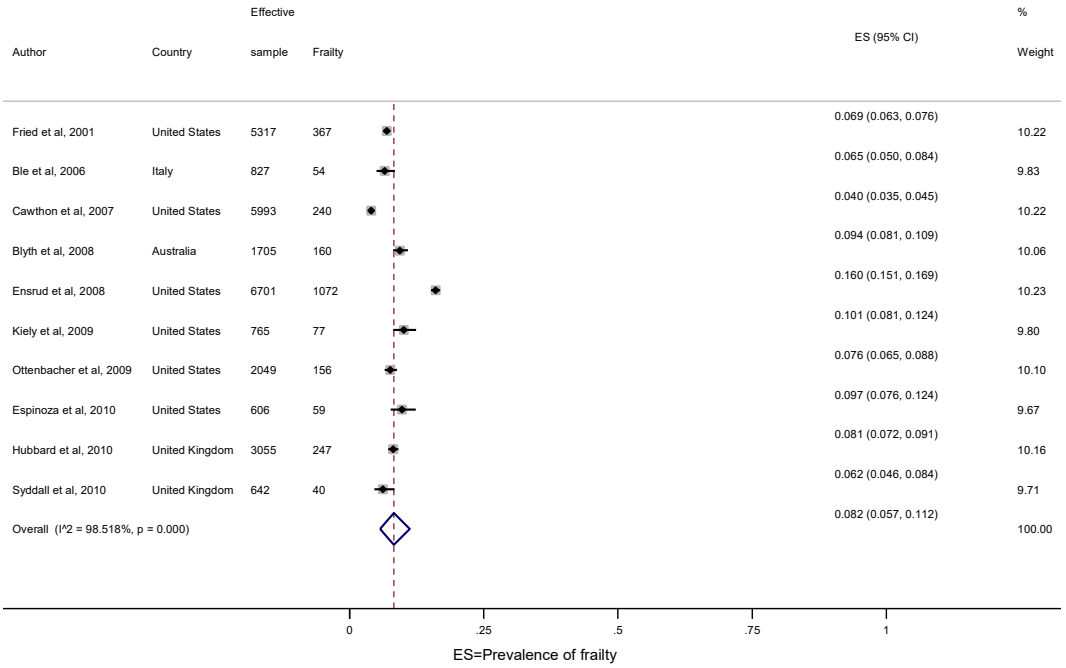
Appendix F: Pooled prevalence of frailty by age and sex for studies using all 5 Fried phenotype criteria with objective assessment for weakness and slowness



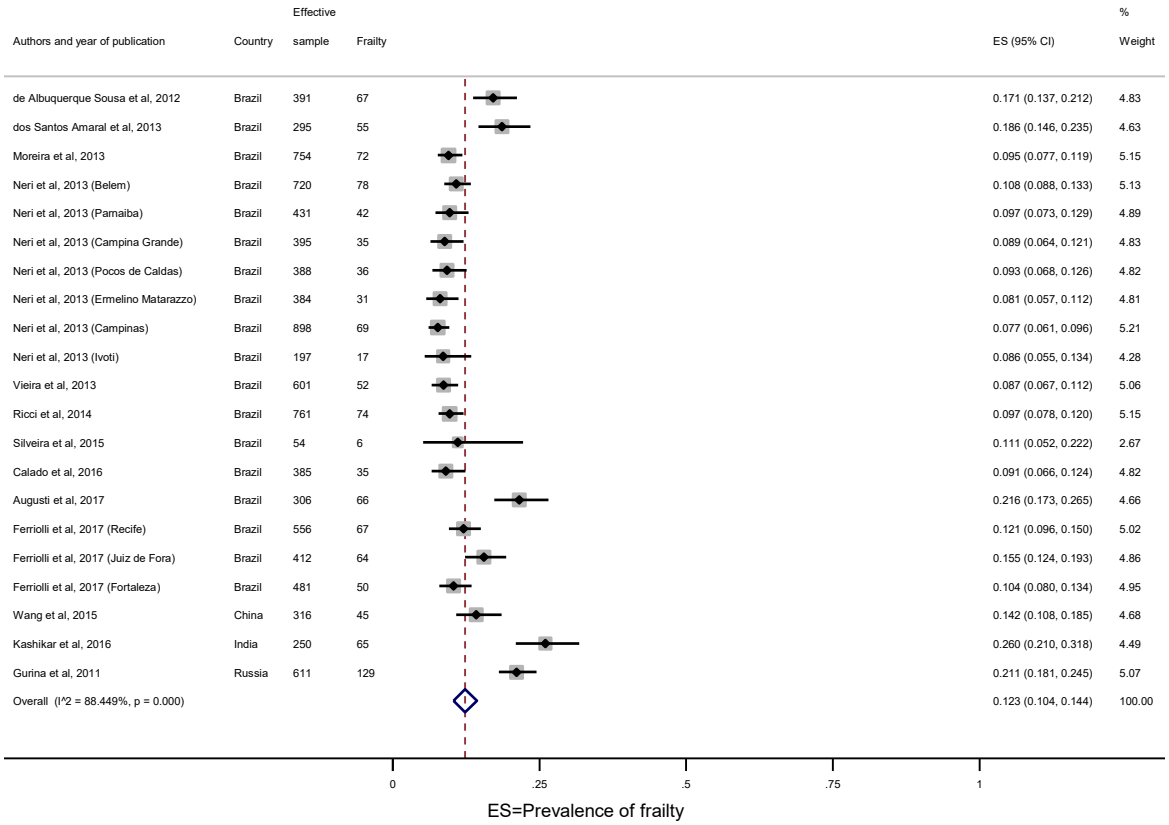
Appendix G: Pooled prevalence of pre-frailty by age and sex for studies using all 5 Fried phenotype criteria with objective assessment for weakness and slowness



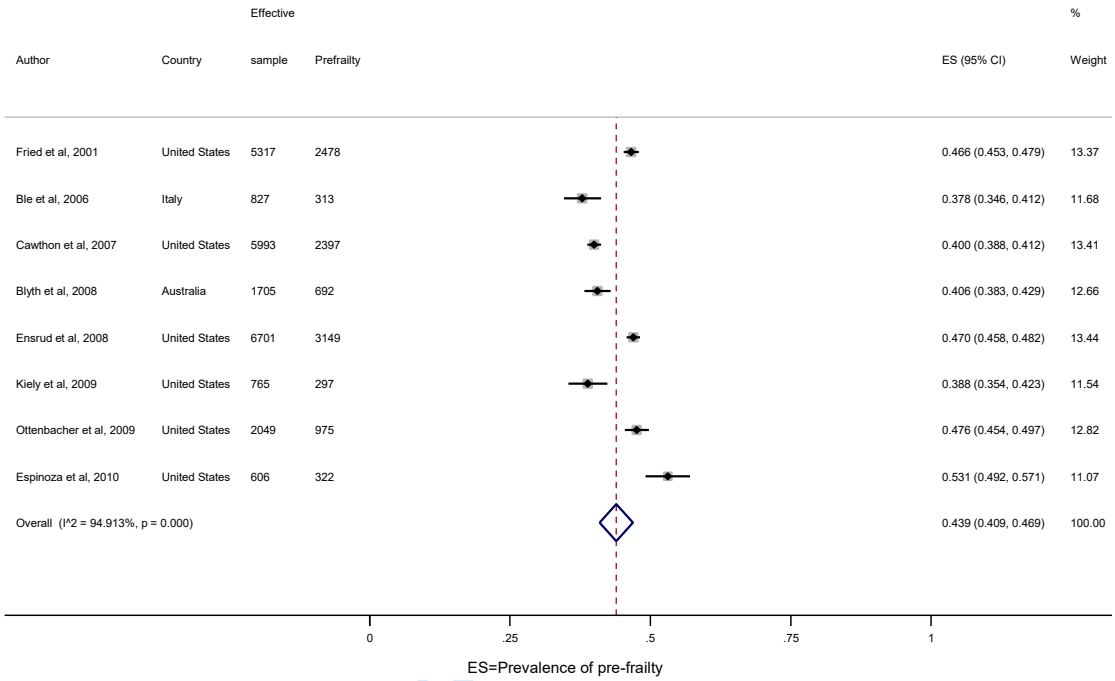
Appendix H: Random effects pooled prevalence of frailty among community dwelling older adults in high income countries



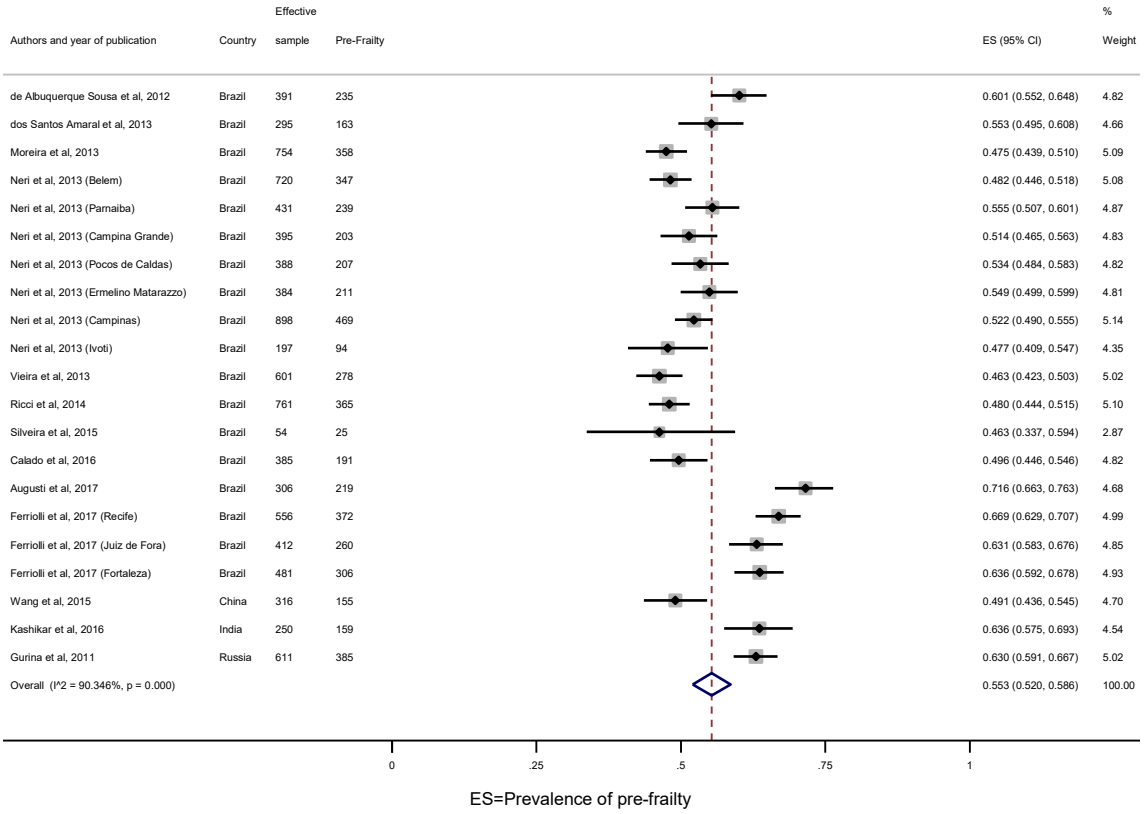
Appendix I: Random effects pooled prevalence of frailty among community dwelling older adults in middle income countries (only with the studies of minimum recruitment age 65 years)



Appendix J: Random effects pooled prevalence of pre-frailty among community dwelling older adults in high income countries



Appendix K: Random effects pooled prevalence of pre-frailty among community dwelling older adults in middle income countries (only with the studies of minimum recruitment age 65 years)



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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	2,10
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6-7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary file, appendix A
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7-8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7-8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8-9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9-10
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10-11
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	11, 14,15 Supplementary file, appendix C
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Supplementary file, appendix B
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	12,14,15 Supplementary file, appendix C
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	12, 16
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	12,13,16
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	16-19
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	20
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	23
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	23-24
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	28

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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